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IN ITS

CLINICAL & PATHOLOGICAL ASPECTS

HANSEN & LOOFT

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WITH NUMEROUS PHOTOGRAPHS AND COLOURED PLATES.

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AUTHORS' PREFACE.

As it is evident in the numerous recent publications on Leprosy that our first work on the disease, which was published in Norwegian, is unknown to many investigators, and as there appear in their publications many statements, to our thinking, premature and founded on insufficient knowledge, we think it desirable to present a comprehensive statement of the result of our studies of this disease, so interesting in itself and so instructive in other directions.

Since one of us has been for more than twenty years occupied in dealing with the disease, we hope to be able to lay before experts a thorough, complete and instructive demonstration, the more, as we do not base our views, as has been frequently and unfortunately done, on any single or scattered observations.

TRANSLATOR'S PREFACE.

IN the translation of this little work I have, of course, made absolute accuracy of meaning my first aim. It presents the views of one who in his knowledge and experience of the disease is probably second to none. There are, of course, certain points on which there is much difference of opinion. For example, Hansen's view, which is very widely held, of the position of the bacilli in the cells, is very strongly opposed by Unna. Then as to the occurrence of nodules on the palms and soles which Hansen denies, Unna remarks that it is quite exceptional, while Hillis seems to consider it by no means rare. The chapter on Treatment has been wholly re-written for this edition, and is practically a summary of the late Dr. Danielssen's views. The photographs are a further addition to the original German edition. It has been pointed out to me that Dr. Hansen does not refer to the recent Indian Commission. His views on it may be found in the *Lancet*, of October, 1893.

In conclusion, I have to thank my friends, Dr. Colcott Fox for a general reading of the proofs, and Drs. George Mackay and Stockman for their revision of those parts relating to the affections of the eye and te the drugs used in treatment.

NORMAN WALKER.

EDINBURGH, *May*, *1895*.

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LEPROSY:

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Chapter I.

INTRODUCTORY.

THE Bacillus Lepræ has now been recognised in all leprous products, and although the fact has not yet been experimentally demonstrated, we may practically say with confidence that Leprosy is a chronic disease caused by the Lepra bacillus.

Leprosy appears in two forms, which are clinically pretty sharply distinguishable, and were named by Danielssen and Boeck "nodular" and "anæsthetic." This nomenclature, introduced by these authors in their pioneer work, *Om Spedalskhed*, Christiania, 1847, *Traité de la Spedalskhed*, Paris, 1848, is so far important as it characterizes the common and most prominent symptoms of the two forms, viz., in the one, the nodular eruption on the skin,

in the other, the anæsthesia which results from the widespread affection of the nerves. On the other hand, regarded from a strictly scientific standpoint, the nomenclature is scarcely the happiest: firstly, because the one form is named from the eruption on the skin, and the other from the results of the affection of another organ, the nerves; and secondly, because the nerves are affected in the nodular as well as in the other form, though the result of the affection, the anæsthesia, does not so dominate the appearance of the disease.

As Danielssen and Boeck recognised, skin eruptions are present in both forms, and since, as we shall later point out, the eruptions differ both clinically, and also somewhat in their anatomical formation, it would perhaps be more strictly correct to describe the two forms as Lepra tuberosa (tuberculosa) and Lepra maculosa or lævis. But, in the first place, it is of questionable advantage to change a universally accepted nomenclature; and secondly, it is very frequently the case that one sees the patient for the first time after the disappearance of the macular eruption with anæsthesia only, so that the name Lepra anæsthetica exactly describes the case. But in order to give to the skin eruption in the anæsthetic form its proper place in the nomenclature we will describe the two forms of the disease as *Lepra tuberosa* (tuberculosa), and

Lepra maculo-anæsthetica. And thus we hope to have done justice both to the founders of the scientific study of Leprosy, and to the clinical appearances of the disease.

Danielssen and Boeck have also described a mixed form of the disease, in which nodular Leprosy is combined with anæsthetic. Sometimes the skin eruption disappears and the nodular form passes into the anæsthetic, and sometimes, though much more rarely, the anæsthetic into the nodular; and since, further, the two forms are so different in their clinical appearances that they look almost like different diseases, the recognition of a mixed form might appear to be justified. But since every case of nodular Leprosy is accompanied by affection of the nerves and anæsthesia; and the natural termination of every case of nodular Leprosy is to pass into the anæsthetic form, if only, as occasionally happens, the patient live long enough; and since the skin eruptions of the maculo-anæsthetic form are characterized, just as those of the nodular form, by the presence of the leprosy bacillus, we regard the transformation of a case of maculo-anæsthetic into nodular Leprosy only as a sign of the unity of the two forms, and we delete altogether the name of mixed Leprosy. Otherwise every case of nodular Leprosy must, at all events after some years of existence, properly be called

"mixed," for in such cases anæsthesia is never absent.

It has been attempted to indicate as a special form of the disease a Nervous Leprosy, in which no characteristic skin affection is present.[1] In view of what we have noted above, that nerve Leprosy is present in both forms of the disease, and that an eruption may be noted at some period in all carefully observed cases of the disease, this attempt to indicate a special nerve Leprosy is evidently wrong.

We will first of all discuss separately the two forms of the disease, the nodular and the maculo-anæsthetic, and then proceed to demonstrate the unity of the disease in spite of the differences in form.

[1] See Neisser: Lepra in Ziemssen's Handbook.

Chapter II.

NODULAR LEPROSY.

NODULAR Leprosy *(Lepra tuberosa, L. tuberculosa)* is usually easily diagnosed by its characteristic skin affection.

The leprous nodes or nodular Lepromata are of different size and colour; their consistence is at first firm and hard; they are but slightly compressible, and show little elasticity. Their form is usually semi-spherical, but they are often oblong. The smallest nodule that we have seen was not more than 1-2 mm. in diameter, and its appearance was so little characteristic, that we had to confirm the diagnosis by excision and microscopical examination. The larger the nodules, the more characteristic is their appearance. As they are almost always seated in the cutis, the epidermis over them is stretched and shiny; it is occasionally normal in colour, but usually at first reddish, later becoming yellow. *The localisation of the nodules is usually characteristic.* They are generally first evident on the face, on the backs of the hands, and on the dorsal surfaces of the wrists, and next on the extensor surfaces of the limbs. They are more

rarely seen on the back and nates; on the flexor surfaces of the extremities, on the breast, abdomen, scrotum, and penis, they are quite exceptional; and we have never seen them on the glans penis, the palms or soles, or on the hairy scalp. Leloir has described a leprous affection of the palms of the hands, of which he himself says that it closely resembled a syphilide in that situation. Since Danielssen, with his enormous experience, never saw a leprous affection of the palm of the hand, we incline to believe that the affection which Leloir observed, not only resembled, but actually was, a syphilide.

Here in Norway where the people often go barefoot, wading in streams, marshes and rivers, the backs of the feet and the under part of the calves are frequently the seat of the first leprous eruption, not so often in the form of nodules, as of a dense, regular infiltration. Now since, as we have noted above, the face and back of the hands are the usual seats of predilection for the earliest appearance of the eruption, it appears not improbable that this has its explanation in the climatic influences on these parts, possibly influenced by the structure of the skin, especially the cutaneous vessels. That there are peculiarities in the structure of the tissues, which determine the localisation of the poison, one may conclude; for certain organs are never affected

with leprosy, in spite of the fact that the poison has evidently at some time circulated in the blood.

The face is usually especially characteristic, as the eyebrows are almost always the seat of nodules. The nodules are sometimes isolated though close together, sometimes there are only one or two, though usually several, and sometimes there are no distinct nodules, but the eyebrow is infiltrated both in length and breadth, and of a reddish colour. Even if the infiltration is not so great that the brow appears thickened, the reddish colour and the shadow over the eyes give to the face a characteristic expression, and one can feel the infiltration, if the brow is gripped between the thumb and forefinger. In these cases the hairs persist; in more severe infiltration, and where nodules are formed, they drop out. The forehead and cheeks usually present a diffuse or spotty redness and burnish, and with the finger one recognises the infiltration as an increased resistance. This discolouration is most evident on changes of temperature, as when a patient comes from the outside cold into a warm room. Not infrequently the suspicion of Leprosy is aroused by this change of colour, and by the shadows over the eyebrows, even years before more definite symptoms appear. But in most cases one finds distinct nodules in the eyebrows

and over the countenance generally. When the nodules are numerous and large, so that the eyebrows project far over the eyes; when the cheeks and chin are beset with large rounded or flat nodules pressing on each other, so as to cause deep furrows between them; when the point of the nose, the alæ nasi, and the lips are infiltrated throughout their whole thickness; the countenance is frightfully deformed, and there is developed the so-called *Facies Leonina.* The lobules of the ears are almost always infiltrated, and become red, thick and elongated. *Plate I* is a case of tuberous leprosy of two years' duration, the hands being swollen with leprous infiltration.

The eyes are, in the nodular form, almost always affected; nodules are frequently present in the eyelids, the upper as well as the lower, and are usually situated close to their margin. The earliest affection of the eye itself, which we have observed, is a faint clouding of the upper part of the cornea, which often appears as a very fine dotting of the corneal surface, only noticeable when one can compare the upper part of the cornea with the black pupil, and often requiring for its recognition the use of a lens. A slight infiltration of the limbus conjunctivæ is always combined with this clouding of the cornea, but it is at this early stage so slight that it cannot be noted clinically. Later on it increases,

PLATE I.

and gradually attacks the whole of the outer margin of the cornea. When this infiltration becomes greater it appears yellow, as seen through the conjunctiva running intact over it, and this gives to the eye a peculiar woe-begone aspect. It is quite exceptional for this infiltration to extend completely round the cornea, for that part of the limbus directed towards the nose is almost always free. As time goes on the infiltration increases, and a low rampart is formed around the cornea. Sooner or later the infiltration and nodule formation attack the cornea itself, in one of three different ways: first, quite superficially, immediately under the epithelium. The nodule in this case is always elevated, usually grows very rapidly till it finally covers the whole cornea, and may by its height prevent the closure of the lids. That part of the cornea lying below or behind the nodule is quite clear. Secondly, the infiltration may attack the cornea in the form of a wedge, and form a node which is not so much elevated as in the previous instance; and thirdly, the infiltration may penetrate the cornea close in front of Descemet's membrane. The result, complete blindness, is the same in all cases when the nodule covers the pupil. A frequent accompaniment of this form of the disease is iritis, or, as anatomical investigation shows, irido-cyclitis. These forms of iritis run a chronic or sub-acute

course, sometimes so stealthy and painless that it is observed by neither doctor nor patient, until adhesions have formed between the pupillary border and the capsule of the lens. Blindness may sometimes be caused by exudation into the pupil. *Plate II* shows a typical case of tuberous leprosy of six years' duration. The hairs have completely disappeared from the eyebrows; on the chin a few can still be seen between the tuberosities. In the right eye is a nodule, growing from the *Limbus conjunctivæ* into the cornea. Nodules may also be present in the iris, and usually arise in the outer and under margin, in the angle between the cornea and the iris; they may completely fill the corresponding part of the anterior chamber, are of a yellow colour, and sometimes look exactly like an obliquely-placed hypopion, as they have an inner or upper straight, or slightly concave margin. We once did an iridectomy directly through a small early nodule, and put a stop to its further growth. On anatomical examination we also find a leprous affection of the anterior part of the retina over the ciliary body, which appears as a fine white spotting of the retina; the ciliary nerves are always for a considerable distance backwards infiltrated with leprosy, as are the *membrana supra choroidea* and the choroid itself.

On the extremities the nodules always appear

PLATE II.

singly, but when closely set may run together to form large plaques. On the backs of the hands and fingers nodules are very frequently, and on the extensor surfaces of the thighs and the front of the legs almost always, found. The calves are often also infiltrated as a whole, especially on the fibular side close above the ankle, and this infiltration reaches as high as the middle of the leg; the skin is tense and shiny, reddish blue in colour, and in this infiltrated part ulcers resembling varicose ulcers readily appear, which are as difficult, if not more so, to heal. They are surrounded by thick elevated walls, may last for years, and occasionally completely surround the leg.

Of the mucous membranes, those of the nose, mouth, larynx and pharynx are affected. The nasal mucous membrane is affected only in its anterior part along with the alæ nasi and the anterior part of the septum. If a general infiltration takes place in this situation, the softening and ulceration which may ensue lead eventually to the disappearance of all the soft parts of the nose; the bones are never affected. (See *Plate III*, a case in which the leprosy developed in 1848, and was of the tuberous variety. The tubers disappeared partly by suppuration. In 1857 he entered an asylum and then presented the same appearances as in the photograph. He was then

anæsthetic. There were cicatrices in the face due to the disappearance of the nodules, the point of the nose was gone, but the nasal bones were intact, thus differing from syphilis. He died in 1885.) In the mouth, the mucous membrane of the lips, of course, shares in the process when these are completely infiltrated, and even on the mucous membrane of the cheeks one occasionally sees and feels thickening and infiltration. The tongue is often the seat of nodules, which in all respects correspond to those of the skin. The gums, the velum, and the uvula may be either infiltrated or dotted with nodules. The rest of the mucous membrane of the pharynx is more frequently infiltrated than beset with nodules, and the same is true of the epiglottis, which sometimes becomes quite stiff and almost immoveable. In the larynx, the true and false cords are more frequently the seat of infiltration than of nodules; the voice is rough and hoarse, the rima glottidis is often so narrowed that respiration is rendered difficult; excessive narrowing of the rima is only present in the late stages, and is proportionately rare. When the mucous membrane ulcerates the cords grow together, both anteriorly and posteriorly, and when the infiltration disappears there remains a scar tissue, which, by its contraction, reduces the rima to a small slit, a few millimètres wide. In

PLATE III.

such cases a very little mucus is sufficient almost or completely to close the opening, and the patient may perish from suffocation. Usually an emetic suffices to open up the hole at once; but tracheotomy is often necessary to supply air to the patient, the attacks of suffocation are so frequent, and since he is already voiceless, he loses nothing by the operation.

The lymphatic glands (cervical, axillary and inguinal) in relation to the affected skin and mucous membrane are always swollen: this leprous swelling is always indolent, and never goes on to suppuration. Sometimes the glandular swelling may aid in the diagnosis, if the skin affection is not absolutely characteristic, though this is most rarely the case.

The nodules are almost always seated in the cutis, but they may, though rarely, be placed deeper in the subcutaneous connective tissue; they form then no projections, but the skin over them is almost always somewhat hyperæmic and bluish-red, and, if the finger is passed over the place, the thickening or the nodule may be felt *in* the deeper parts. It is in our experience that a patient who had only this form of nodules was regarded by a colleague, well acquainted with the disease, as free from Leprosy, probably because he did not use his fingers.

From the symptoms described above, the

diagnosis is almost always very easy, and we ourselves know of no disease of the skin which can be confounded with nodular leprosy. If necessary a piece of skin may be removed and examined for the presence of bacilli, which, at least in the nodular form of the disease, are never absent. This we have once had occasion to do.

In addition to the skin the nerves are also affected, not always at the commencement, but always in the later stages. Whether all peripheral nerves are affected we cannot say—certainly the facial, radial, ulnar, median and peroneal are always diseased. According to our investigation the nerves of the extremities are affected throughout their whole length, but the affection is severe only at certain places, viz., where the nerves run superficially over bones or joints, as the median at the wrist, the ulnar at the elbow, and the peroneal where it crosses the fibula. As a result of this nerve affection we have pain followed by anæsthesia. The pains in the arms, hands, feet and calves are sometimes very severe and persistent. The affection at first causes pain, by pressure on the nerves, and later—when the pressure has led to atrophy—anæsthesia. Now since, as we shall later clearly demonstrate, leprous affections tend to heal, it is not infrequently the case that nerve affections, when slight, pass off without having specially

injured the nerves, and these nerves may be the seat of fresh infections, and thus the patient suffers from repeated painful attacks through a course of years. This is particularly the case where there is general infiltration of the legs, and is either the result of repeated attacks of the same, or of the implication of different nerve branches. The nodules are often painful when first developed, but later on sensation is deadened.

Of internal organs, the testicle, liver, and spleen, are always affected in this form, but we shall consider them later in the description of the pathological anatomy.

Before we more closely describe the course of the disease, we shall first briefly discuss the fate of the nodules. These usually remain for years unchanged, growing very little or not at all. The skin over and around them, or rather its vascular supply, is very sensitive to changes of temperature, so that the skin, as we have already indicated, changes its colour with change of temperature from dilatation of the blood-vessels. The vessels evidently suffer from the invasion of the leprous poison. New outbreaks have often the appearance of an "erythema nodosum," with great hyperæmia. We had once the opportunity of examining a piece cut out of such an erythema-like eruption, and found dilated vessels and round cells, and only after long search a few bacilli.

One must conjecture that there is deposited with the bacilli a chemical poison which affects the vessels, or that the bacilli produce the poison, and that this poison has its action only in its immediate neighbourhood.

But occasionally the nodules grow so luxuriantly that the epidermis develops furrows and clefts which may reach down to the nodules, and then a bloody fluid comes out of them which dries up on the surface to a reddish brown scab. Or it may happen that the upper horny layers of epithelium disappear, and that only a few rows of cells of the rete Malpighii remain. In this case the exuded fluid less often dries, the surface is usually blood-red and moist, and appears like an ulceration, though it is not really one. When this takes place on the face, particularly on the lips, or on the backs of the fingers, the sufferings of the patient are very much increased. After several years the nodules usually soften about the middle of their base, and the nodule may sink in over the softened part; or they burst, the softened part is thrown off, and now is developed the true ulceration by which the nodule may be completely eliminated and sunken stellate scars alone remain.

The determination of the commencement of the disease is exceptionally difficult, indeed impossible, for it must always be founded on the

statements of the patient, and the patients either observe themselves insufficiently, as may frequently be noted, or they conceal many facts. As a matter of fact we do not know the earliest symptoms of the disease. According to Danielssen and Boeck, the patients often suffer long and repeatedly, before the outbreak of the disease, from weakness, with rheumatoid pains and fever. This the patients frequently corroborate. But we are inclined to regard these attacks of fever as indications of the already existing disease. It appears to us more probable that the disease begins with some form of local affection which is so indistinct that the patient himself does not notice it, or at least lays no weight upon it, and that these local affections are analogous to others with which we are familiar, namely, the nodules which may last for years before new and such definite eruptions appear, that the disease cannot any longer be ignored or kept secret. We believe therefore, that the patients do not really know when they commence to be ill, and that they date the beginning of the disease from a later eruption. If at the commencement only the extremities are affected the patients may conceal their condition for years, and through this concealment become so accustomed to lie, that later it is impossible to receive from them correct information.

The cases are very frequent in which the

patients have for several years only scattered nodules, and then suddenly a fresh outbreak of numerous nodules. The disease always advances by outbreaks of eruptions which repeat themselves at longer or shorter intervals. It is very often the case that the older nodules soften during a fresh outbreak, and completely or partly disappear; and these outbreaks are always accompanied by fever, the temperature rising to 39° or 40° Cent. Now we know that the nodules, if the patient is affected by another febrile disease, may disappear. It is, therefore, difficult to decide whether the disappearance of the nodules is the cause or the result of the eruptive fever. But we possess certain observations in which the disappearance of the nodules has begun before the onset of the fever, and in which, therefore, the fever and the later eruption appear to be caused by the softening of the nodules. Supported by these observations we regard the eruptions as auto-infections, in which bacilli (or poison) from the older lepromata pass into the blood, and thus new areas of the skin or other organs are affected. We have often observed that an iridocyclitis, or an affection of the throat, arises during an eruption, and also that the nerves beneath the nodules become swollen and painful, and once we have seen the testicle become swollen and painful during an eruption. As to the affections of the liver and spleen we

have no clinical observations ; they appear to cause no clinical symptoms, or at all events, such indefinite ones that, although our attention has been directed to them, they have escaped observation.

The eruptions are of the most varied duration. Some last only a few days and cause so little fever that the patients experience no particular disturbance to health ; they only know that a few new nodules appear, or that they are sore about the throat. Others last for weeks, indeed, months, with remittent fever, the temperature rising to 40°. Quinine has no effect. During such eruptions the strength of the patients is of course distinctly diminished, but when the eruption is over they recover rapidly and feel themselves all right again ; only they are more leprous than before, or at least have more leprous manifestations. The number of eruptions varies greatly in different cases. Sometimes the patient has, for several years, several eruptions every year ; in other cases the eruptions appear only very rarely—one or two in the whole course of the disease, and they may be very slight. It appears as if the bacilli in different cases were of varying virulence, or possibly the structural conditions are different in different individuals, so that in some the bacilli (or the poison) reach the blood more easily than in others.

Therefore the *fate of the patient is very*

different. If the eruptions are frequent the growth of the nodules is usually luxuriant, and those nodules with diminished epithelial covering, and therefore moist, are very frequent. If then, the whole countenance and part of the extremities are covered with such nodules; if the eyes are blinded by the formation of nodules in the cornea; if the tongue and the pharynx are, through formation of nodules and infiltration, half ulcerated and sore; if respiration is made more difficult by the narrowing of the rima, and the voice inaudible; then the condition is as miserable as is possible to conceive.

If there is added to this, amyloid degeneration of the kidneys, liver, spleen and intestine, with diarrhœa, it can only be desired that death shall put an end to such a condition, and that usually takes place soon, although occasionally the patient may linger for months. Whether leprosy alone is responsible for the end is, we think, doubtful; as remarked above, the affections of the liver and spleen appear to be without much significance.

The biliary secretion is never influenced, and there is according to our observations no special leprous anæmia. The patients are indeed often anæmic, or become so during the disease, but we have not been able to convince ourselves that this is a direct result of the leprosy. In many examinations of the blood, which were indeed under-

taken for other purposes, we have never noticed anything remarkable in relation to the number or form of the blood-corpuscles.

As in almost all cases of nodular leprosy nephritis is present, we are inclined to regard this nephritis as a frequent cause of the marasmus which ensues. Tuberculosis was formerly a frequent occurrence in our hospitals, where our observations have chiefly been made. The relationship between this and leprosy we will discuss later.

The prognosis in the case of patients in whom the eruptions appear less frequently is more favourable, and they may live many years. Either they die from an inter-current disease or as a result of their nephritis, or they become in time anæsthetic, that is, according to our view, they recover. When the nodules become stationary they ultimately soften, as described above, and may be absorbed without opening, though this is rare and usually occurs only with single nodules; or they burst and ulcerate; in either case they leave scars. If this takes place in all the nodules and the patient is attacked by no fresh eruptions, then anæsthesia gradually develops as the result of the affection of the nerves; in the nerves, too, the specific leprous affection disappears, and there remains only scar tissue, which by compression

destroys the nerve fibres and thus causes anæsthesia. Then gradually all specific leprous affections disappear, and the patient is healed from his leprosy, and may live many years in perfect health, having lost practically nothing of his power of work. Such cases are unfortunately not very frequent; but we have had the opportunity of examining some after death and have not been able to discover in them any specific leprous affection.

Thus one is struck with the fact, how little leprosy of itself influences the health of the patient, and if nodular leprosy usually shortens life, that takes place probably because in this form the frequent ulceration leads to amyloid degeneration of the internal organs, or that the nephritis is a sequel of the leprosy. The nephritis appears either as the so-called parenchymatous or as the interstitial; according to our examinations it is never bacillary. Further, as nephritis is very much rarer in the maculo-anæsthetic form of the disease, it must be assumed that nodular leprosy in some way causes nephritis. The same is true of amyloid degeneration. The duration of life of a patient with the nodular form of leprosy is in general eight to nine years after the definite outbreak of the disease.

The most frequent complication which we have seen in our institutions is tuberculosis, particularly

some years ago, for then the institutions were over-crowded, and consequently the sanitary conditions were in many respects unsatisfactory.

In order to give an idea of the frequency of this complication, we have placed in tabular form at the end of this work the results of eighty-nine autopsies (see TABLE I, page 128).

From the statistics there given it is evident that we have had ample opportunity of examining the combination of tuberculosis and leprosy. Most of these examinations were indeed made in the pre-bacillary era ; but we are satisfied that the *differentiation* of tuberculosis and leprosy without an examination for bacilli is by no means difficult.

As Danielssen and Boeck had described a leprous affection of the intestine, we gave great attention to this point, and as we were at the same time engaged in an investigation on the pathological anatomy of the lymphatic glands, we lost no opportunity of carefully examining these organs. It was during this investigation that we discovered the characteristic leprous affection of lymph glands, and had our attention first directed to the leprous affection of the liver and spleen, which affections are, macroscopically, so little evident, that we at first overlooked them.

The leprous and tuberculous affections of the lymph glands are macroscopically so very dif-

ferent, that it is impossible to confuse them, and the microscopical differences are still more evident. Both fresh and hardened preparations were always examined. And since the lymph glands are always affected with leprosy, if the organs which drain into them are affected, even if this affection is very slightly developed, we conclude from the fact that we have never seen a leprous bronchial or mesenteric gland, that there is no leprous affection of the lungs or of the intestine, and later examination of certain special preparations have only confirmed us in this view. But more of this later, and we will first treat of the differences between tuberculosis and leprosy.

In organs affected with tubercle one always finds, as is well known, giant cells and caseous degeneration ; in the many, we can truthfully say, thousands of preparations of leprous affections, which we have had under the microscope, we have never seen either a typical giant cell with marginal nuclei or caseous degeneration. There are indeed multinuclear cells in the lepromata, but never giant cells like those of tubercle.

What may be the reason for this striking difference in the action of the very similar bacilli of tubercle and leprosy, we have no idea ; we simply state the fact and assert that, if one finds giant cells, he is dealing with tuberculosis and not with leprosy. This alone would be sufficient

to cause us to separate the two neoplasms, but there are many other distinctions. Tubercle is avascular; the leproma is rich in vessels; tubercle undergoes caseous degeneration, the leproma never. Anatomically therefore, we are justified in maintaining a sharp distinction between the two diseases.

So far as concerns the resemblance between the tubercle and lepra bacilli, we must not omit to mention that one almost always finds among tubercle bacilli some which are pretty long and somewhat bent; this is never the case among lepra bacilli. Baumgarten has indicated as a distinction between them, the fact that the latter is more easily stained; according to our experience this distinction can scarcely be regarded as sufficient. But the distribution of the bacilli in the tuberculous and leprous tissue is usually so very different, the tubercle bacilli being usually arranged singly, the lepra bacilli always in large quantities in masses and clumps, that a confusion of the two diseases anatomically can only be possible in exceptional cases. Danielssen has repeatedly stated in his triennial report of the Lungegaards Hospital that tuberculosis and leprosy are such nearly allied diseases that the one (leprosy) may pass into the other (tuberculosis) by a modification of the bacilli, and that thus the frequent combination of the two diseases

is to be explained. This view we cannot, in view of the above demonstration, support. If an organ is attacked at the same time by tuberculosis and leprosy, one can anatomically very readily separate the two diseases. We would rather seek the explanation of the frequent combination of the two diseases in our institutions in the great overcrowding and consequently insanitary conditions to which they were formerly subjected. Tuberculosis once introduced, we find a ready explanation in the bad habits of the patients in regard to expectoration, why it was difficult or impossible to root it out. In later years, when the institutions are no longer full and the sanitary conditions consequently much improved, tuberculosis has much decreased. Whether tuberculosis was as frequent a combination in the country as in our institutions we do not know. The duration of life of patients in the country is about a year longer than in our institutions, and possibly this depends on the absence of tuberculosis.

Doutrelepont has recently described in the transactions of the German Dermatological Society, *On the Pathology and Therapeutics of Leprosy*, a lung affection, probably developed by tuberculine treatment, which he diagnosed from the examination of the sputum. But the patient had a leprous affection of the larynx, and his account by no means excludes the possibility that

the bacilli in the sputum came from a ruptured nodule in the larynx, possibly softened by the tuberculine treatment. We cannot, therefore, recognise this observation as infallible evidence of the presence of a leprous lung affection, any more than that case of leprosy of the lungs described by Bonome in *Virchow's Archiv*, Bd. C. That author himself draws attention to the great resemblance of the affection to tuberculosis, and as it is quite evident from his description of the bronchial lymphatic glands that they were not leprous, and he notes the presence of giant cells in the pathological products, we cannot doubt that it was really a case of tuberculosis.

In the same case there was found an affection of the spinal cord, from which Bordoni-Uffreduzzi cultivated on glycerine agar an organism which he recognised as the lepra bacillus. Here we may remark in the first place that we have never seen a leprous affection of the spinal cord, and have never found bacilli in it. We must indeed admit that we have only examined the spinal cord in a few cases, because there appeared to be no indication for such an examination, since clinical symptoms do not point to an affection of that organ, and as in the profusely nodular cases, affections easily recognised appear everywhere, except in the liver and spleen, it was to be expected that an affection of the spinal

cord would have been recognisable. In necrotic bones, which we have often examined, nothing leprous is found. This necrosis is therefore no specific leprous affection, but a secondary one. Secondly, we must remark that in spite of many attempts we have never succeeded in cultivating lepra bacilli on glycerine agar. We therefore believe that Bordoni-Uffreduzzi has cultivated tubercle bacilli instead of lepra bacilli. The only thing which speaks for the leprous nature of the lung affection and the cultivated bacilli, is the circumstance that the author did not succeed in inoculating guinea pigs and rabbits with tuberculosis. But, according to all investigations on tuberculosis, it appears to us not incredible that the tubercle bacilli may, under circumstances, become so weakened that they are no longer pathogenic.

Arning has described a miliary leprosy, and found in the products of this disease giant cells, and also leprous ulcers in the intestines. Dr. Arning has kindly sent us some preparations of this miliary leprosy, in which we find evidence everywhere that the case is one of tuberculosis, both because giant cells are found everywhere, and the bacilli are only present singly, and scattered. They are never present in the excessive numbers, and have not the arrangement, which they usually have in leprous products. In connection with the

presence of giant cells in leprous products, we may note that we have received from two foreign colleagues preparations in which they believed giant cells to be present. But we have found, on careful examination of the preparations, that they were cross and oblique sections of blood vessels, which with their endothelial nuclei gave the impression of giant cells. Without the use of a homogeneous immersion lens it was not possible to make a definite distinction.

According to our observation there exists a sharp anatomical distinction between leprosy and tuberculosis, and there is no such thing as leprosy of the lungs and intestines, the bones and the kidneys. In order to establish a differential diagnosis in doubtful cases, we recommend in the case of the lungs and the intestines a thorough examination of the bronchial and mesenteric glands. We ourselves have never sought in vain, in cases of these affections, for tuberculous or caseous degeneration in the glands, and we have seen in no single case anything resembling leprous affection of the glands.

So far as concerns the central nervous system, Danielssen noted that he had several times seen acute hydrocephalus in leprosy. We once saw severe cerebral symptoms with maniacal attacks. The patient, who was taken into a lunatic asylum, left this later, cured. Other indications of an

affection of the central nervous system in leprosy are unknown to us. Anatomically, we have not been able to recognise in the nervous system any traces of leprosy. In connection with this, we may note that we have several times seen pain and swelling of the knee joints during eruptions, which at their conclusion disappear. In these cases there is nothing to be made out anatomically. When we reflect that, as indicated in describing the eruptions, the bacilli and (or) their toxines most probably circulate for some time in the blood, it is remarkable that the organs above referred to are not affected by leprosy. We can give no reason for this ; connective tissue, which is especially liable to be affected, is present everywhere.

Chapter III.

STRUCTURE OF THE LEPROMA.

THE leprous nodes have on section a smooth, white, glistening surface, if they are still sufficiently young. If one examines, microscopically, sections or teased preparations of fresh nodules, one sees little else but cells, with distinct nuclei, usually of the size of a white blood corpuscle, or rather larger. There are also a few larger so-called epithelioid cells, with larger nuclei, and among the cells, fragments of connective tissue and of blood vessels. With a higher power, one sees in the fluid of the preparation small straight rods, which are not destroyed by addition of potash. These are the lepra bacilli, and thus were they first discovered in the year 1871.

If one teases out preparations in osmic acid solution, or soaks a nodule in the solution some hours before teasing, the rods are coloured faint brown, and one finds them lying mostly in the cells (*Plate VI, Fig.* 1). If one adds water to a fresh preparation, the bacilli move actively; even in the cells swollen up with water, one sees the bacilli moving; and this led us to regard them as movable, although we at the same time indicated

a doubt whether the movement was not simply a molecular one ; for the movements were equally vigorous in strong osmic acid solution as in water, and on the addition of glycerine or strong solution of albumen to the preparations, the movements ceased. All later observers, with the exception of Unna, regard the bacilli as motionless. We have no ambition to decide this question, because we know no absolutely trustworthy distinction between molecular movement and independent movement of the bacilli.

The older the nodules become, the more large multinuclear cells are found, and in nodules of the skin and cornea one always finds small flat cells with processes, and with oblong nuclei, which we recognise as the connective tissue and corneal cells (*Plate VI, Figs.* 2 and 3).

The protoplasm of these cells is clear, while that of the round cells is more or less granular. The nuclei of the latter are also round, and usually very granular ; the flat cells are much less stained by carmine than the round cells, and one sees the flat cells lying on connective tissue bundles. The nodules are richly supplied with blood vessels; in the nodules of the skin it cannot be determined whether the vessels are newly formed, or only those already present in the cutis. They are, however, always of embryonic type. One sees very plainly their formation from cells,

and in the cornea, indeed, the vessels *must* be newly formed. Here the vessels penetrate into the cornea before the nodule forms, and round these vessels, penetrating into the cornea, there are always visible collections of cells which are apparently migrated white blood corpuscles (*Plate VI, Fig.* 4).

One meets also in old nodules, among apparently only unproductive elements, blood vessels surrounded by young cells (*Plate VI, Fig.* 5). This appears definitely to favour the view that the tumour cells are, at least for the most part, migrated blood corpuscles. These results have been obtained by examination of fresh nodules, and of those hardened in Müller's fluid. As we have recently, while hardening the nodules in Fleming's chromic and osmic acid mixture, and staining the sections with hæmatoxylin, been unable as yet to find any mitoses, and further, have found, by bacillary staining of an old section from a corneal node, an appearance like *Plate VI, Fig.* 7, we must maintain provisionally that in the lepromata the new formations are, at least chiefly, formed by the immigration of white blood corpuscles. As the round cells infiltrate the connective tissue, the fibres are pressed asunder, and form a network closely resembling that of a lymph gland with nuclei in the angles (*Plate VI, Fig.* 6).

When the nodule softens, which takes place almost always exactly in the middle, it attains a brownish tint, which is due to the transparent softened part. If one divides the softened nodule, the central part has a distinct brown colour, and the constituents of this part readily fall out. If this is examined under a microscope, one sees, almost exclusively, larger or smaller clumps of a brownish colour, and very granular. They are partly elastic, but partly brittle and fragile, so that by pressure on the cover glass they are easily broken up. One often sees clearly that the clumps lie *in* the cells, the nucleus and the cell substance being still evident (*Plate VII, Fig.* 1). Sometimes only one lies in a cell, which then has the appearance of a signet ring, in whose circle the clump lies, but sometimes several lie in one cell. One finds similar clumps in all other organs affected with leprosy, as in the liver, the spleen (*Plate VII, Fig.* 2), the nerves, lymphatic glands, the testicle and the eyes (*Plate VII, Fig.* 3, which shows two clumps from the retina). In the nodes of the skin, but particularly in the testicles, one may find them so large that they may even be seen by the naked eye. Both in the small and the larger clumps there are usually vacuoles, not infrequently several. From the cornea we have often got preparations in which the corneal corpuscles are more or less completely

filled with brown granules (*Plate VIII, Fig.* 1). One sees here definitely the cell nucleus in the middle of the brown granular material.

We have described these elements as we first observed them in fresh and carmine-stained preparations, in which they stand out very definitely, as the brown masses do not take up the carmine stain. These brown elements, if one knows their characteristic appearance, may very well serve as diagnostic indications for leprous affections, for, according to our experience, one never fails to find them except in very young nodules. Since the discovery and easy recognition of the lepra bacillus, they have indeed lost their value as diagnostic signs, unless one is examining perfectly fresh preparations. Later investigation has proved that these brown clumps are nothing else but collections of lepra bacilli broken down into granules, and they have received from Neisser the well-chosen name of "globi," as they usually appear in spherical form. Unna declares, in accordance with his view of the position of the lepra bacilli outside the tumour cells in the lymph spaces, that these "globi" are collections of bacilli in the lymph vessels, and that the vacuoles have arisen from the falling out of bacilli in the middle. In particular, Neisser, Touton, and we, ourselves, have opposed this view, in that we have all seen the bacilli definitely in the cells, and have figured them

so. In view of the above description of the discovery of bacilli in fresh preparations and of these brown clumps, there can scarcely be any doubt of the position of the bacilli, and of the cellular nature of the brown clumps. Further, it may be noted that in the testicles the "globi" are chiefly in the lumen of the seminal canals, where no lymph vessels exist, and if Unna says of the "globi"* that "no one has certainly determined their cellular character," he must have said this in ignorance of our earlier publications in Norwegian. The above description and the drawings were published by us in 1869 and 1870, in the *Nordiskt Medicinsk Arkiv.*

In connection with the vacuole, we have found in a testicle a "globus" with vacuoles, and in the vacuoles small granules which were recognised as remains of the nuclei (*Plate X, Fig.* 2). We add to this the picture of a "globus," or rather a developing "globus," with two nuclei, from a skin nodule (*Plate VIII, Fig.* 4). We have seen earlier, however, that the brown clump may lie in the cell without enclosing the nucleus, and also that the nucleus may lie in the middle of the brown mass. Now, if the vacuoles are transformed nuclei, as we believe, then it would be comprehensible that the

*Unna, zur Histologie der Leprösenhaut; in Leprastudien, Monatshefte für practische Dermatologie, Ergänzhungsheft, 1885.

vacuoles would be absent in many "globi," and that in others which have developed from multinuclear cells, several vacuoles would be found. That appears, at least, the simplest explanation of their presence. But there are certain very small "globi" with vacuoles, such as are represented in *Plate VII*, *Fig.* 2, *c*, and those small vacuoles can scarcely represent nuclei; small "globi" may however arise, as is evident at x and x^1 of the same figure, from clumps of bacilli in the cells. The vacuoles of the larger "globi" of x and x^1 may indeed possibly represent nuclei, but not the vacuoles in *Plate VII*, *Fig.* 2, *a—k*, nor the vacuole in one of the small "globi" in x^1. Possibly the vacuoles are also the result of a specific degeneration, either of the bacilli themselves, or of the cell protoplasm lying in the middle of the group of bacilli, but on this we would rather not express an opinion.

We have repeatedly demonstrated the position of the bacilli *in* the cells, and explained them in diagrams, but in many preparations it is impossible to distinguish where the bacilli lie. The best method of definitely noting their position, which we know, appears to be the fixing of small nodes or small pieces of organs in Fleming's or Müller's fluid, with subsequent dehydration and hardening in alcohol; sometimes one gets excellent preparations by simply hardening in absolute

alcohol. If the preparations are stained with fuchsin, and counter-stained with methyl blue, or still better, stained with gentian violet, decolourised by Gram's method, and counter-stained with Bismarck brown or with Bismarck brown and eosin, one will never fail to see the bacilli lying definitely in the cells (*Plate VI, Fig.* 8). Even in such preparations there are many places where one cannot definitely distinguish the position of the bacilli ; but as one always finds bacilli in the cells where the preparations are sufficiently clear, we may safely conclude that the bacilli lie everywhere *in* the cells. In the connective tissue spaces one often sees bacilli in and round the nuclei of the connective tissue cells (*Plate X, Fig.* 8), and although the body of the cell is not visible, we may conclude that the bacilli lie in the cell body, and not free in the lymph spaces. We have found in many sections of the blood vessels in a testicle (*Plate X, Figs.* 5 and 6), and in a liver (*Plate VIII, Fig.* 6, and *Plate IX, Fig.* 1), white blood corpuscles filled with bacilli, and in both cases only slight affection of the organ, and we also observed many bacilli in the endothelium of the vessels, as Touton and Unna have observed in skin nodules where we, we may remark in passing, have never seen them. From these observations we draw the conclusion that these two organs have been infected through the blood. As we do not know the

manner and method of the primary infection of the organ, we must devote our attention to the search for discoveries like those described above, and to the localisation of the bacilli in general, in order to form an idea of the method of action of the bacilli.

As we have already noted, we found in the examination of an excised piece of a recent eruption, in a nodular case of leprosy, chiefly, round cells surrounding dilated vessels, and only after long search, a few bacilli. It thus appears not improbable that during the eruption a toxin (which is circulating in the blood), and only a few bacilli, escape from the vessels at various places, or, it may be, only the bacilli, which produce the toxin locally ; that further, the toxin causes the emigration of white blood corpuscles, and that the escaped bacilli only after some time slowly increase in number and gradually fill the cells. From the presence of the bacilli in the endothelium of the vessels and in the connective tissue cells, one may speculate that the bacilli are passively forced into them by the blood or lymph pressure ; we have certainly found, in the testicle referred to, bacilli free between the red blood corpuscles in the vessels (*Plate X, Fig.* 7). Such a fresh eruption may remain stationary or slowly develop into a nodule, or it may apparently completely disappear, and only after several years again become

apparent, it may be during a fresh eruption. We fancy that in these cases a few bacilli are deposited at the time of the first eruption, and that they have needed years to become so much increased that a permanent nodule has finally formed. That the vessels receive lasting injuries from the leprous infection, appears to us to be proved by the following observations. In an epidemic of measles in one of our institutions, we saw in anæsthetic patients the previous leprous spots, which had long disappeared from view, definitely reappear, the *hyperæmia* and turgescence being on these places general, so that the earlier spots stood out as well defined, red, and somewhat swollen areas. All this appears to point to the fact that the bacilli increase very, very slowly, and that possibly they also produce a toxin, usually only in small quantities, which causes no particular injury to the organism, since the patients, in spite of numerous nodules with millions or milliards of bacilli, may remain in pretty good health for years. We may also conjecture that the toxin which is produced, usually only acts immediately around the bacilli, leading to dilatation of the vessels and favouring the migration of white blood corpuscles. Only occasionally does the production of toxin or the multiplication of the bacilli appear to become so vigorous that toxin and bacilli get into the blood and cause an eruption ; possibly this is favoured by

peculiar anatomical conditions, for it is very striking with what varied frequency eruptions appear in different patients. That the bacilli in the nodules are all of them dead, as has been assumed, we cannot admit, so long as the nodules still grow. It appears to us preferable to ascribe the character of the disease to the relative benignancy and slight viability of the bacilli, as Unna has already suggested. As we believe, as explained above, that the bacilli lie almost exclusively in the cells, the question arises whether the cells digest the bacilli, or not. As we often find cells with only one or two bacilli, and as we find in most cells balls or clumps of bacilli, we must admit that the bacilli multiply in the cells. In some cells the bacilli remain lying in separate collections, in others they fill the entire cell body, but they never penetrate into the nucleus. Finally, the bacilli break down into small granules, and this breaking down corresponds, according to our view, to a degeneration of the bacilli. Unna and Lütz have indeed stated that this granular appearance of the bacilli is constant, and is a mark of their structure, that they really consist of small rows of cocci, and Unna has therefore described them as coccothrix. This actual (!) structure of the bacilli, however, only becomes evident under the action of free iodine. But we have seen in our preparations, however they were treated, *smooth and granular bacilli*

lying close to each other, and we cannot, therefore, corroborate the view of Unna and Lütz.

Neisser first drew attention to clear spaces in the bacilli ; these Neisser regards as spores ; we regard them as the first sign of breaking down of the bacilli into granules, and for the following reasons. We have made numerous attempts to cultivate the bacilli, and have attained in all our investigations only (the breaking down of the bacilli into) granules, and in examining a piece of a nodule which lay eight days on broth peptone agar, found all the bacilli beset with clear spaces. And as the result has always been the breaking down into granules, we believe we are right in regarding the appearance of these holes as the commencement of degeneration, and that we are not as yet familiar with spores of the lepra bacillus. It appears as if all bacilli in time break down into granules, particularly in the internal organs, where it occurs much earlier than in the skin nodules ; whether this is the result of digestion on the part of the cell, we cannot say ; but as the bacilli at first multiply in the cells, and the breaking down appears most definitely and freely when the cells are crammed full of bacilli, it is equally possible that it is the result of diminished nutrition, and as they break down more rapidly in the internal organs, it is also possible, indeed probable, that the higher temperature in these

organs favours this disintegration. As we have unfortunately not been able to cultivate the bacilli, it is at present impossible to form a conclusion. At all events, we regard the transformation into granules as a degeneration, and believe that the bacilli thus altered are dead.

In the skin nodules we have only once found bacilli in the epidermis; this was in a nodule with many fissures in the epithelium, and partly covered with exudation. We have not been able to decide from our preparations whether the bacilli lie *in* the epithelial cells or only *between* them, possibly enclosed in wandering cells.* Touton found bacilli in the epithelium of the sweat glands, and he and Unna in the hair sheaths also; this situation of the bacilli we have never observed with certainty, and it can only be exceptional, and can scarcely give origin to a "constantly flowing bacterial spring," as Unna suggests. As a rule, no bacilli are found in the epithelium.

Of the presence of bacilli in affections of the eye, it may be said in general that everywhere, where infiltration is present, bacilli are found. In the clouding of the upper part of the cornea described

*In a nodule, with exudation, which we have recently examined, we have found bacilli in the epithelium, and there are in several places distinct leucocytic nuclei in the bacillary groups, thus showing emigrated cells with bacilli in the epithelium.

above, which we recognise as keratitis punctata, there are found groups of granularly degenerated bacilli close under the epithelium. This we have only once been able to determine on the living by excision of a lamella of the cornea; in this case the affection was, according to our own view, disappearing, because the bacilli were granularly degenerated. This corresponds with the fact that this characteristic affection of the cornea always ultimately disappears ; the granules are probably absorbed. We have already stated that blood vessels precede the nodule into the cornea, and that they are surrounded by round cells. Here, as in the middle of the nodule, the corneal corpuscles are found apparently intact or filled with brown granules (*Plate VI*, *Fig.* 3, and *Plate VIII*, *Fig.* 1). The same is the case in nodules in the iris, in which one finds the stellate cells intact (*Plate VIII*, *Fig.* 2). Round cells are also found in the spaces in the cornea near the nuclei of the corneal corpuscles (*Plate VIII*, *Fig.* 3). All this appears to us definitely to indicate that at least most of the cells of the growth are migrated white blood corpuscles.

Dr. Boeckmann has introduced, in the treatment of the nodules growing into the cornea, the division of the cornea in front of the nodules ; through the scar formed by the healing of the wound, they hardly ever grow. We have seen such a case in

which, on the one side of the scar, no actual nodules, but only a clouding appeared, and we were later able to examine the eye anatomically. The nodule reached like a rampart close up to the scar, and all its cells were full of bacilli. On that side of the scar in the clouded part of the cornea, there were found only a few scattered cells containing bacilli ; no vessels had penetrated the scar, and only a very few cells had succeeded in making their way through. The treatment is therefore a very desirable one in order to preserve the pupil free. We have been able to prepare no bacillary preparations from the *retina*, as we have not seen the affection since the discovery of the bacilli ; the two brown clumps which are figured in *Plate VII*, *Fig.* 3, lay in the outer granular layer of the retina.

As already indicated, the testicles are affected with leprosy in all nodular cases. The affection is both inter-tubular and intra-tubular. In a testicle only slightly affected, we found bacilli everywhere in the endothelium of the vessels, and in several dilated vessels white blood corpuscles filled with bacilli (*Plate X*, *Figs.* 5 and 6) ; and in some places also bacilli lying free between the red blood corpuscles (*Plate X*, *Fig.* 7). At the same time, and especially where the affection is more marked, the bacilli penetrate into the seminal canals, and lie grouped in their walls around the nuclei (*Plate IX*, *Figs.* 4 and 5, *Plate*

X, *Fig.* 1), and their epithelial cells are more or less filled with them (*Figs.* 1, 2 and 4).

The bacilli appear rapidly to break down into granules, and one finds, especially in the seminal canals, globi, sometimes enormously large, as if they were formed by the running together of several epithelial cells. We have found here globi where a nucleus and a little protoplasm were evident (*Plate X*, *Fig.* 3), and a globus where there lay in the vacuole small fragments stained with Bismarck brown (*Plate X*, *Fig.* 2). As it has been proved that a man affected with nodular leprosy may beget children, and as the globi lie in the seminal canals, it is not altogether impossible that these may be thrown off with the spermatic fluid, and that in this way the ovum is infected. But as, according to our view, these globi contain only broken down and degenerated bacilli, it must be regarded as very doubtful whether they are still infective. In examining the contents of the seminal vesicles, we have found in them neither bacilli, nor globi, nor any spermatozoa. It is an old conception that lepers suffer from satyriasis. This is, according to our experience, certainly not the case. The leprous testicle is finally completely destroyed by the scar-like contraction of the connective tissue, and one finds only here and there traces of the seminal canals around the globi which they enclose.

When the liver is severely affected with leprosy, there are evident macroscopically, fine white, or yellow, streaks or points, which shine through the capsule and are more evident on the cut surface (*Plate IX, Fig.* 2); they evidently lie in the acini. One also finds round cells with bacilli along the portal vessels and in the capsule of Glisson. Here and there we find also scattered bacilli in the acini, and as is evident from a specimen hardened in Fleming's solution, the bacilli lie in the endothelium of the blood vessels (*Plate IX, Fig.* 1). In the liver cells we have never seen bacilli, but we have found here also, in the vessels, white blood corpuscles containing bacilli (*Plate VIII, Fig.* 6, and *Plate IX, Fig.* 1).

The affection of the spleen may also be recognised macroscopically by the yellow streaks and points in its substance (*Plate IX, Fig.* 3), but the affection must be pretty severe to be recognised macroscopically; the cut surface is then somewhat dry. The affection has its seat in the arterial sheaths and the Malpighian bodies; and in this organ also one can in good preparations definitely recognise the position of the bacilli in the cells (*Plate VIII, Fig.* 5).

The glands in the hilum of the liver are, when that organ is affected with leprosy, definitely leprous, and the affection of the glands is often more evident than that of the liver itself. In the

hilum of the spleen we have once or twice found leprous lymph glands.

This leprous affection of the glands is macroscopically very readily recognisable. The glands are swollen as a whole, without any alteration in their form. On section, one sees the ampullæ and the medullary cords of a yellow or yellowish brown colour; this colour gives to the glands such a characteristic aspect that they can hardly be mistaken. The affection is best studied on the inguinal glands, and the retro-peritoneal ones in connection with them. The lowest inguinal gland is always most swollen, reaching sometimes to the size of a pigeon's egg; the ampullæ and trabeculæ are coloured throughout a deep yellow; but the somewhat thickened capsule and the connective tissue framework have retained their greyish semi-transparent appearance, so that the structure of the gland stands out very clearly, especially if the lymph sinuses are injected with blood pigment, which is sometimes the case when there have been peripheral hæmorrhages in the nodules. As we advance upwards the glands are gradually less swollen, and the yellow colouring of the ampullæ and trabeculæ less intense, and one can further follow in the retro-peritoneal glands a gradual diminution of the affection until, about the level of the kidney or rather higher, normal glands are once more met with. The glands are

permeable, but penetration is evidently more difficult, for the lymph vessels leading to them are dilated, especially those of the lowest and most swollen glands.

With great patience and moderate pressure one can succeed in artificially injecting the lymphatics without causing extravasation. It may even be the case that only one, or at most one or two ampullæ are affected. Microscopically the ampullæ and trabeculæ are found more or less filled with brown bodies or globi. These are evidently lymph cells which have become filled with bacilli and their degenerative products—granules.

One could hardly have a better demonstration of the functions of the lymphatic glands, as filters, than in these leprous glands. The circulation through them is not arrested; nevertheless, the glands retain the infectious product, and if it pass one gland it is arrested and retained in the next. Sometimes the quantity of this infection is so small that one or two ampullæ are sufficient to retain the whole of it. This indicates that the circulation in the gland does not take place exclusively through the lymph sinuses, but that the lymph reaching the gland must at once enter the ampullæ. A similar process is seen in tubercular lymphatic glands, in which one often finds only one or one or two ampullæ infiltrated with tubercle.

In the nerves the bacilli are found partly in round cells, which lie around the vessels and between the nerve fibres, and partly in the cells of Schwann's sheath; here also they break down into granules, and in time completely disappear. The finer details of the affection of the nerves are best studied on the ciliary nerves when the eye is affected, because there one can examine the finest nerves without cutting sections or putting them through any manipulation which might injure them. One often sees the myelin sheath pressed in by bacilli or cells filled with granules (*Plate XII, Fig.* 2), and one finds nerve fibres without a myelin sheath and with a more or less atrophic axial cylinder (*Plate XII, Fig.* 1). These drawings clearly explain how the pressure on the axial cylinder at first causes pain, and later, when atrophy has set in, anæsthesia. And one can also understand that when the leprous affection passes off without complications, the axial cylinders are again restored and become functionally active.

But on those places above referred to, where the nerves run superficially over bones or joints, and are exposed to pressure and stretching, secondary inflammation is added to the process.

While the primary leprous affection hardly appreciably thickens the nerves, the secondary inflammation causes a very marked thickening.

The ulnar nerve at the elbow may attain a diameter of 7 to 8 mm. or more, and when the secondary inflammation disappears the connective tissue contracts, and the previously thickened nerve becomes thinner than normal. This whole process usually advances very deliberately, and years are required before anæsthesia is developed to its full extent. While the section of the thickened nerve is quite smooth and of a pale brown colour from the numerous globi present, the section of the atrophic nerve, though also smooth, is as pale as the section of a tendon. It consists almost exclusively of connective tissue; every trace of bacilli has disappeared, and one sees hardly a suggestion of nerve fibres. The leprous affection is healed, but only a completely functionless rudiment of the nerve remains.*

*Just as the manuscript of this treatise was completed, a year and a half ago, we obtained at an autopsy a lung in which there was tuberculosis, but at the same time probably leprosy also. Most unfortunately the bronchial glands were not preserved for microscopical examination. Dr. Lie also permits me to state that he has found leprosy bacilli in two kidneys and in one lung. He had diagnosed tuberculosis of the lung, but at the autopsy he found only an indurating pneumonia, containing lepra bacilli, and no tuberculosis. In the kidneys, of the same case, he found lepra bacilli in the glomeruli, and in the interstices between the cortical tubules. He will describe the case more fully later. This is a mere preliminary note.

Chapter IV.

LEPRA MACULO-ANÆSTHETICA.

THIS form of leprosy was first distinctly and well described by Danielssen, who called it *L. anæsthetica*; but since the macules, as Danielssen recognised, play an important and constant *rôle* in the course of the disease, we prefer the name maculo-anæsthetica, as it includes the two most striking symptoms; the name *L. nervorum* used by many investigators, we do not consider satisfactory. Certainly the nerves suffer most, and the neuritis is the most prominent feature in the disease, but the skin affection is a bacillary one, which precedes or accompanies the neuritis; it is *not*, as is often believed, a tropho-neurosis, as we have determined by the demonstration of bacilli in both young and very old leprous patches.

Thus there disappears the sharp distinction between the two forms of the disease—the tuberous and the maculo-anæsthetic. We must regard them as the same disease, only with varied intensity in the action of the bacilli.

One can distinguish in the maculo-anæsthetic form, different stages in the course of the disease,

but in general they cannot be very sharply defined from one another.

In the prodromal stage, which is of very varied duration, lasting for months or even years, the patients state that they suffer from exhaustion, general debility, rheumatoid pains of the joints or muscles, hyperæsthesia of the skin, neuralgic pain of certain nerve regions, sopor and mental depression. Ephemeral eruptions of spots are admitted; and pigmentary anomalies, sometimes atrophic, sometimes hypertrophic, were noted by Bidenkap.

Danielssen states that he has seen, at the very beginning of the disease, a slight vaso-motor disturbance, which is indicated by a bluish-red reticular appearance, which is evident most clearly on changes of temperature. These vaso-motor disturbances, which appear as slight patches which can be induced by friction, are chiefly characteristic of the maculo-anæsthetic, though they may appear during the earliest stage of the tuberous, form.

In fact, our view is that the so called prodromal symptoms are nothing more than the earliest, indefinite, undiagnosable phenomena of infection.

One or more eruptions of pemphigoid bullæ may occur in the commencing stage, but we have more often seen them later, both accompanying the

patches and in the stage of anæsthesia and mutilation.

After a longer or shorter period the typical picture of the maculo-anæsthetic form develops; the spots either appear stealthily or they may appear all at once with marked fever. Several forms of the eruption are described by investigators; in our patients usually only the erythematous and the yellowish or brownish pigmented ones have been noted. Usually both forms are seen on the same patient, for the simple erythematous spots become in time more and more pigmented—usually only at the periphery, where a bluish red play of colours is often seen. Those eruptions which are all along pigmented and which develop very gradually, we have particularly noted in the intercostal spaces. Various forms—round, oval, gyrate—have been observed. The patches may be perfectly flat, or slightly elevated. The size varies from that of a pea up to that of the palm of the hand, and they may be even larger. At the commencement, we have usually found these patches hyperæsthetic; anæsthesia is only found in the older patches. They do not always at once attain their full size; we can often observe their growth; one may run into another, and then the initial form is lost. The number and extent of these patches are very varied; some patients present great map-like eruptions on the face, back

PLATE IV.

and extremities ; in others the patches are few and scattered. The seat of these patches corresponds in general to that of the nodules, but the back and the intercostal spaces are frequently the seat of patches, while on these areas nodules are only rarely, if ever, present. *Plate IV* gives a good picture of the patches in the maculo-anæsthetic form—duration, two years. The white centres and the slightly elevated reddish edges are very well shown. A symmetrical distribution of the patches strikes one, and has been regarded as indicative of a central localisation of the leprous poisons of which the patches are a tropho-neurotic vaso-motor symptom ; but in many cases there is absolutely no symmetry, and the discovery of bacilli in the patches themselves proves them to be the direct result of the action of the lepra poison. The lymphatic glands corresponding to the position of the patches are always swollen, and the swelling may persist long after the disappearance of the patches. The duration is very varied ; some are gone in a few days or even less, others may last for years. Pigmentation of the periphery and pallor of the centre indicate that the patch is already old, and the pallid centre is always anæsthetic, the anæsthesia affecting all, or only some perceptions. The signs which Hillis indicated, as diagnostic of the patches of the anæsthetic from those of the tuberous form, we

cannot recognise. The patches of the tuberous form are certainly usually thicker, indicating a greater degree of infiltration, than the anæsthetic ; but as both are caused by the lepra bacillus it is evident that they may be absolutely similar.

The longer the disease lasts the more does the neuritis predominate ; the ulnar and peroneal trunks may be felt to be thickened, they are sensitive to pressure, and, if carefully felt for, the peripheral finer branches may be felt as delicate thickened cords. In one case we were able to feel the cutaneous nerve branches in a patch, growing daily more and more thickened, in contrast to the large not especially affected nerve trunk. The large palpable nerve trunks are not equally thickened in their whole length, but the thickening appears about the joints where the nerves run across bone.

The symptoms of this neuritis are various ; at first neuralgia, and later, widespread anæsthesia, with trophic disturbances, such as the formation of pemphigoid bullæ ; we have often seen hydrarthrus and pains in the joints. Motor pareses and paralyses are never absent, but they are not, as Neisser argues, due to a leprous affection of the muscles, but are a secondary neuritic symptom, as we have discovered from anatomical examination of the muscles. As the neuritis especially affects the peripheral nerve trunks, we find the secondary

symptoms in the peripheral regions, usually only in the extremities and on the face. We will now more closely consider the various nervous symptoms.

Neuralgia is usually present in the extremities, in the ulnar and peroneal regions. The anæsthesia relates to the different qualities of sensation, and is not only present in the patches, but progresses gradually from the periphery toward the centre, so that at last the whole extremity, and often also parts of the trunk, become anæsthetic ; the face is always more or less anæsthetic. We have often found thermal anæsthesia present alone, or accompanied by anæsthesia or analgesia. The anæsthesia may become more and more extensive, or it may very gradually disappear, indicating that the neuritis of the affected nerve has disappeared.

Trophic and vaso-motor disturbances are never absent if the neuritis is pronounced and lasts for any time ; the skin may become œdematous, or it becomes thin, shiny, and slightly scaly (glossy skin). We have often seen, especially if the neuritis has lasted long, and the later symptoms such as mutilation have commenced, dark-coloured hyperkeratoses, usually symmetrical on the front of the leg, or on the dorsal surface of the hands. In one patient we observed on the toes horny, thick (1·5 cm.) symmetrically placed formations,

which when thrown off left a new-formed rosy-red skin, with intact sensibility; the patient had on the front of the leg the appearances of ichthyosis.

The changes in the nails are a part of the trophic disturbance; they become thickened, brittle and cleft, and sometimes thin and diminished in size, as one finds them, as we shall see later, in the terminal stages. The secretion of sweat is affected, being diminished over the anæsthetic areas, and the hairs there are altered and fall out.

We regard the pemphigoid bullæ as a trophic symptom; they may appear at the very commencement of the disease, along with the macular eruption; but they usually appear late when the anæsthesia has become extensive; in this we agree with Danielssen. Neisser and Leloir give prominence to the early appearance of pemphigoid bullæ, Neisser believing that the irritation of the commencing interstitial neuritis causes this trophic symptom. Our reason for regarding them as trophic symptoms is that we have never been able to find bacilli in the bullæ we have examined, not even in those which appeared at the same time as the maculæ, and their marked symmetry is also in favour of their nervous origin. The bullous eruptions usually appear suddenly. The patients will discover on awaking, one or more blisters which may be already burst; some have pain and fever for hours or days before their appearance;

(Leloir). They vary in size—they may be small, from the size of a pea to that of a bean, or as large as the palm of the hand.

Their contents are serous, but if the bullæ persist, they become purulent. They usually rupture early and heal, leaving behind them violet-coloured scars, which after some time become pale. If irritant factors are added, if the bullæ last long and become purulent, there develops after rupture deep ulceration, most frequent on the hands and feet.

Bullous eruptions of the mucous membranes, which Leloir has noted, we have never been fortunate enough to see.

We regard also as tropho-neurotic vaso-motor symptoms the acute rheumatoid affections of the joints, which are not infrequent in our hospital. The joints, especially the small ones of the fingers and hands, and also those of the knee and ankle, become painful and tender, and on palpation, a collection of fluid can usually be recognised. The affection is always symmetrical.

These affections of the joints, which belong to the earlier stages of the disease, usually appear simultaneously with the macular eruption, and disappear with it, but they may appear later; and after one, or it may be only after several attacks, thickening of the ends of the bones and ligaments, with stiffening of the limbs, is developed. Leprous

affections of the tendon sheaths, which Wolff refers to, we have never seen. The contracture of the fingers and toes is not tendogenous, so far as we can decide from clinical and anatomical investigation; it is myogenous, the leprous paralyses, which we shall immediately describe, being the cause.

Hillis claims to have recognised a motor weakness in the prodromal stage of the disease, and considers that the nerves are already affected with the leprous virus. Such a weakness referable to a neuritis of the motor nerves we have not noted previous to the macular eruption and the onset of the anæsthesia. If there are, in the prodromal stage, muscular weaknesses, we are inclined to regard these as symptoms of the general weakness; according to our view, the skin affection is the *first* definite symptom of the disease. The muscular affection may always be definitely recognised as a secondary symptom by the atrophy, and the altered electrical reactions. Different degrees and varied extent of the muscular affection may be noted; trivial paresis with only very slight atrophy, which, along with the anæsthesia, may completely disappear, if the neuritis passes off without destroying the nerve fibres; and almost complete paralysis with great atrophy of the muscles.

Paralysis with atrophy is most marked on the

PLATE V.

hands and forearms, feet and calves, and on the face.

The interosseous muscles of the hands and feet atrophy, so that the interosseous spaces appear as furrows. The thenar and hypothenar muscles also disappear, and the first interosseous space becomes a depression. The muscles of the forearms and calves also atrophy and lose their power, but complete paralysis is never developed ; the patients can always move their hands and walk. In the face, all the muscles atrophy and lose their power, and thus all expression is lost. The masseter muscles occasionally, though very rarely, become so atrophic, that the lower jaw drops, and must be retained in position by a bandage. Paralysis of the *Orbicularis Oris* leads to dropping of the under lip, and to extreme difficulty in closing the mouth, and consequent escape of saliva. (See *Plate V*—a case of maculo-anæsthetic form completely cured and anæsthetic. The maculæ were developed in 1857, and the patient is still alive.) Paralysis of the *Orbicularis Palpebrarum* renders the closure of the eyes impossible, and paralytic ectropion of the lower lid is developed. The results of this on the eye we will refer to later. The muscular atrophy is by no means always symmetrical ; one hand may present marked atrophy, while the other is tolerably useful. This indicates the peripheral development of the paralysis, as

does the fact that the muscular sense is preserved, and in particular that no ataxic symptoms appear. The patients can do fine knitting and needle-work with their paretic hands. Their gait has a peculiar character, from the difficulty with which the weakened muscles raise the feet, but they can both stand and walk quite well with closed or bandaged eyes. As we shall see later, this clinical observation corresponds with the results of the anatomical examination of the cord.

Along with the paralysis and atrophy of the muscles, there appear also, as the result of the destruction of the nerve trunks, *trophic affections of the bones and of the skin.* The changes in the skin have been already described; when the anæsthesia is advanced, there always appear ulcerations under the heel and the ball of the foot. Most of these owe their origin simply to pressure; the weight of the body is too much for the atrophic skin. They are always callous, heal with great difficulty, and so long as the patient goes about, not at all. The ulcers are not usually deep, but it may happen that they penetrate as far as the bone, and lead to necrosis. But usually necrosis of the bones is preceded by periostitis, and when the pus makes its way out, an ulceration leading down to necrotic bone is formed. We have sometimes seen the formation of a blister precede the ulceration, but it is rare, and it is cer-

tainly not true, as stated by many authors, that ulceration of the sole is always preceded by a bulla. Not only on the feet but also on the hands, necrosis with exfoliation of bone takes place; the phalanges are especially attacked. When the atrophy of the muscles is advanced, the fingers are always claw-like, with extension of the first phalanx. The joints consequently often *appear* swollen, although no joint affection is present. The phalanges and the metacarpals undergo simple atrophy, becoming very thin at the middle, and since the joints retain almost their normal thickness, they appear swollen by contrast. As already noted, this clawing of the fingers is accompanied by no disease of the tendon sheaths. The bones in the feet undergo the same form of atrophy.

If, in addition to this atrophy of the bones, which was first noted and demonstrated by Prof. Hjalmar Heiberg, there ensues necrosis with exfoliation of whole phalanges or metacarpals (the carpal bones very rarely necrose), there is great mutilation of the hands and feet; all the fingers of the hand may go, and there remain on the diminished carpus only small, soft processes, each supplied with a nail—the remnants of the fingers. The toes disappear from the feet, the metatarsal bones atrophy, and several of the tarsal bones may exfoliate; so that ultimately there remains of the foot only a pyramidal cushion at the lower end of

the leg. In most cases we must regard external injury as the cause of these necroses. The patients feel nothing when they injure themselves; they may burn their hands at a stove without noticing it. Under such circumstances it is not to be wondered at, that inflammation is readily excited, especially as the vitality of the parts is evidently diminished. But it is remarkable how well operation wounds heal. One may do pretty extensive necrotomies, and the wounds heal well and quickly, either by granulation or by first intention. In such operations it is a frequent experience that the bone is reached before the patient feels anything, but he immediately feels pain when the periosteum is scraped or the bone attacked with forceps or saw. We believe, however, that it is only nervous individuals who complain of *pain;* though it is certain that when the bone is meddled with, something is *felt.* Probably in this connection may be explained the statement of the patients, that when walking they *feel* the ground. It is easy to demonstrate that a patient who is quite unconscious of any irritation on his skin, can perceive deep pressure fairly well.

These necroses and trophic disturbances, together with the muscular contraction, cause the *mutilation* characteristic of the last stage of the disease, which was at one time described as a special form, *Lepra mutilans.*

We said above that the finger joints *appear* enlarged on account of the atrophy of the shaft of the bone. In some cases, however, the joints, especially the ankle, show changes which must either be regarded as the remains of the rheumatoid affections of the eruptive period, or as trophic articular changes, corresponding to those seen in *Tabes dorsalis*. We have seen ankles and knees, but especially ankles, presenting such an appearance. In some cases post mortem examination shows widespread tuberculosis of the synovial membrane and of the ends of the bones, which we shall refer to more particularly under the pathological anatomy.

As we have already mentioned, the eyelids can no longer be closed on account of the paralysis of the orbicularis palpebrarum, and consequently the under part of the cornea remains uncovered during sleep. This leads to a punctiform drying of the epithelium of the cornea, and further, to an injection of the conjunctivæ at the under margin of the cornea; then the vessels gradually attack the cornea, which becomes opaque, at first around the xerotic spots, and later in its whole under part. It may go on to ulceration with rupture of the cornea and prolapse of the iris, and finally to complete atrophy of the globe. As a result of the paralysis, the lower lid is always ectropic, at first at its inner end, and later, com-

pletely. As the lower punctum is thus drawn away from the bulb, the tears run down over the cheeks, and the paralysed countenance looks still more woe-begone.

In the later stages, when the facial paralysis is very pronounced, the senses of smell and taste may be very much diminished, or completely lost.

We often see symptoms which are not proper to the disease itself developing during its course, such as obstinate cardialgia, acid pyrosis, and vomiting of a slimy nature indicating gastric catarrh. Diarrhœa or chronic obstruction is by no means rare, nor is albuminuria dependant on parenchymatous, interstitial or amyloid nephritis.

The course of maculo-anæsthetic leprosy is essentially chronic. Cases usually last between ten and twenty years; some may even exceed forty.

The patients often die cachectic, without one being able to find on the post mortem table any definite cause of death, or they may—though in our aseptic and antiseptic times more and more rarely—perish from septicæmia or pyæmia. Pulmonary or general tuberculosis was formerly a frequent cause of death, which, however, usually takes place from some intercurrent disease.

In the ordinary course of the disease the macular eruptions disappear, and the neuritic symptoms—anæsthesia, muscular paralysis and

atrophy, and necrosis of bone—appear. Sometimes, though rarely, there are several macular eruptions after the disappearance of the earlier maculæ, or there may be an eruption of nodules. If, then, these eruptions are auto-infections, they are evidence in favour of the unity of the disease, in spite of the difference in form.

Where the bacilli come from, in these, so to speak, later eruptions, when there is no skin affection, it is difficult to say with certainty. In a case of maculo-anæsthetic leprosy we found the inguinal glands leprous, although no skin eruption was present. Possibly, then, fresh eruptions develop from the glands when the original skin eruption has disappeared. Thus the specific leprous affections gradually disappear, and only their results remain—in other words, *the leprosy is healed.* Most maculo-anæsthetic patients become in time purely anæsthetic; they no longer suffer from leprosy, *but only from its results.* The late eruptions show, however, how difficult it is to define the fact of recovery, for when all externally diagnosable signs of actual leprosy are gone, bacilli may still remain somewhere in the body, in the lymphatics, or possibly in the liver and spleen.

Chapter V.

PATHOLOGICAL ANATOMY OF THE MACULO-ANÆSTHETIC FORM.

THE maculæ exhibit generally the same anatomical characters as do the nodular lepromata, viz., infiltrations with round cells, epithelioid and spindle cells. The difference between them is quantitative; in the macular infiltration the number of bacilli are less. We will describe the microscopical appearance of macules of different duration.

In a *recent* (three weeks old) macule, microscopical examination showed cord-like and rounded infiltrations of the cutis, with round and epithelioid cells, mostly arranged around the vessels. There were *pretty numerous* bacilli lying between and also definitely in, the cells ; here and there were found little collections of bacilli or bacillary granules, with one or more nuclei—small globi —in their neighbourhood, which in size could not be compared with those found in the tuberous form. Specimens hardened in perosmic acid showed unaffected nerve fibres, which the leprous infiltrations did not implicate. Gold prepara-

tions showed a marked increase in the number of Langerhans' cells in the epidermis, which, indeed, we expected, since we agree with Ranvier in considering them as wandering cells, and not as nervous elements. Definite changes in the cutaneous nerves were not evident.

Microscopical sections from an older spot (perhaps two years old) show here and there infiltrations in the cutis—especially around the vessels, consisting of epithelioid, round and spindle cells. Bacilli were found here and there—one or two in each infiltration. In the lumen of one small vessel we found a collection of round cells, with a bacillus among them ; and on the inner side of the wall of another vessel we saw a similar appearance. Gold preparations of this macule, which was definitely anæsthetic, showed slight changes in the small nerve twigs in the cutis, less marked precipitation of the gold salt in the nerve fibres, and a number of Langerhans' cells.

Sections from a very old anæsthetic macule showed only very slight infiltration along the vessels ; the cells were mostly spindle-shaped ; only a few were round or epithelioid. In most of the sections no bacilli were found ; in some, one or two distinct bacilli and some granules, taking the same stain.

The maculæ are therefore like the nodules, leprous infiltrations of the cutis, consisting of

round epithelioid and spindle cells, the latter being more numerous the greater the age of the macule. These infiltrations appear to proceed from the vessels. Lepra bacilli are always present, but are most numerous in the younger macules. In young, not as yet anæsthetic, macules, the nerve twigs appear unchanged; in the older ones they are usually affected. Langerhans' cells are, according to our view, wandering cells, and their number is probably dependant on the inflammation.

We have only had the opportunity of examining the nerves in this form of the disease in old cases, and have not found bacilli in them, but merely great increase of the interstitial connective tissue and disappearance of the nerve fibres. Dr. Arning has, however, as is well known, found bacilli in a piece of ulnar nerve which he removed during life from an anæsthetic patient. Our results, therefore, correspond with the proposition put forward above, that the leprous affection disappears, and that the anæsthesia is a result of the atrophy of the nerves caused by secondary shrinking. We found on a mutilated finger the collateral nerve almost completely transformed into fibrous tissue, not a single medullary fibre being evident. In a case where on account of joint disease (which proved to be tubercular) we amputated, the small periosteal nerve twigs were much degenerated;

in another, where the foot was amputated for gangrene, the small peri-articular nerves also showed degeneration.

Danielssen found, in some cases, changes in the spinal cord which, using the methods of investigation then at his disposal, he regarded as degenerations and inflammations of leprous origin.

Armauer Hansen, Neisser and Leloir have not been able to find any leprous affection of the cord. The cases with changes in the cord, described by Langerhans and Steudener, were, in our view, *not* leprosy. Tschiriew's case, *Lepra tubero-anæsthetica*, presented no marked changes.

Looft has found, in two cases of maculo-anæsthetic leprosy, degeneration of the posterior columns, atrophy of the posterior roots and fibrous degeneration of the spinal ganglia, with disappearance of the medullary fibres, and changes in the nerve cells. In these two cases the affection appeared to be primary in the ganglia, and secondary in the cord. Lepra bacilli were not found in either case, but Chariotti found them once in the cord, and Suderkowitsch in the spinal ganglia.

From all this we can only conclude that the cord is affected in some cases, in others not; *definite clinical symptoms* are absent, and where they suggest a central cause, they may be equally well ascribed to a peripheral neuritis.

The lymphatic glands related to the affected skin are swollen, but not nearly so much so as in nodular leprosy. After death one usually finds the glands but little swollen, and their appearance presents nothing characteristic. In only one case of maculo-anæsthetic leprosy have we found the inguinal glands distinctly leprous, and that two years after the disappearance of the macules. This indicates in the first place that the affection of the glands is due to the same cause in this as in the nodular form, and secondly, that the leprous affection of the glands may last longer than that of the skin. In the same case we found indefinite traces of leprous affection of the liver and spleen, unfortunately so indefinite that we cannot say with certainty whether the liver and spleen are affected with leprosy in this form of the disease. The case occurred in the pre-bacillary era.

The *muscular affections*, paralysis and atrophy, play a prominent *rôle* in the maculo-anæsthetic form of the disease, and the anatomical examination of the muscles is of great interest since some (Neisser)* regard it as a specific leprous process, while G. and E. Hoggan† had previously described it as secondary, and due to the neuritis. In our‡ examination of various stages of

*Virchow's Archiv, Bd. C. III.
†Archive de Physiologie, Bern. 1882.
‡Zeitschrift, par D. C. Danielssen, Bergen, 1891.

muscular atrophy, we have found that the changes begin with a multiplication of the nuclei of the *Perimysium intern.*, which becomes thicker and thicker; at the same time the muscle fibres become thinner, they retain their transverse striation, and some break up into discs. The greater the thickening of the perimysium the thinner become the muscle fibres, so that one must regard the process as an atrophy due to pressure. The intra-muscular nerves showed interstitial neuritis.

Where the atrophy was very pronounced, as in the small muscles of the hands and feet, the muscular fibres had completely disappeared, and only fat and connective tissue remained. We found no bacilli, not even in sections of very early stages of the process, where the larger nerve branches, relating to the part, contained numerous ones, either in so-called mixed or in true tuberous cases. We must therefore with Hoggan regard the muscular affection in leprosy as a secondary one, caused by neuritis. We have tabulated at the end of this work the results of thirty-six post-mortems on maculo-anæsthetic lepers (see TABLE II, page 138).

In those thirty-six cases we find *simple meningitis* twice, *tubercular meningitis* once, *solitary tubercle in the cerebellum* once, and *hydrocephalus internus* twice. The protocol notes nothing further.

The spinal cord twice showed macroscopic changes (thin and atrophic once, thickening and hyperæmia of the lumbar cord once).

The most of these brains and cords, which are entered as normal, were unfortunately only examined macroscopically.

Two cords thoroughly examined by Weigert's method showed degeneration of the posterior columns.

The peripheral nerves were probably examined in all cases, but only the results of a few of the examinations are noted.

The lungs were found tubercular thirteen times, the intestine four times, once without the presence of pulmonary tuberculosis being noted, this making fourteen cases of tuberculosis out of thirty-six —almost exactly 39 per cent. In the nodular form we had thirty-six undoubted tubercular cases out of eighty-nine—rather over 40 per cent. Possibly, and indeed probably, some insufficiently described cases in this form were also tubercular, but the frequency of tuberculosis is so nearly equal in both forms, that there is no ground for supposing that the particular form of leprosy has any relation to the development of tuberculosis. Under precisely similar conditions, in our institution, the nodular and maculo-anæsthetic cases were pretty equally attacked by tubercle. If Leloir means to say that

tuberculosis is much rarer in the maculo-anæsthetic form, than in the nodular, it is certainly not the case in our leper hospitals.

So far as concerns the *necrosis of the bones*, the panaritii and periostitides, we have found in them nothing specific; we have often sought for bacilli, but always in vain. Pyogenic cocci, usually the staphylococcus aureus, we have found both microscopically and in cultivations.

The mutilation of the bones may occur from concentric atrophy alone, as demonstrated by Prof. Hjalmar Heiberg (*Klinisk arbog*, III). The phalanges of the hands and feet, the bones of the metacarpus and metatarsus, and even the carpal and tarsal bones, diminish in all their dimensions, evidently from trophic changes, the result of the neuritis.

We have been able to examine anatomically a few of the cases of articular affection referred to above, but we have not seen instances of the acute affections on the post-mortem table. R. Thoma has described clinically and anatomically a case of *lepra tuberosa* (*Virchow's Archiv*, Bd. 57), in which first the elbow, and later the knee joint, was affected. Examination of the knee joint showed an inflammatory irritation of the nature of hæmorrhagic gonitis. Where we have noted joint affections in the maculo-anæsthetic form we have only noted a condition of hydrops. The chronic

affections we may indicate as tubercular and tropho-anatomical. Tuberculosis attacks the joints of lepers by no means infrequently, as is easily explainable in the case of those already tubercular, by the frequent traumata to which the anæsthetic and paretic lepers are exposed. The carpal and tarsal joints are most frequently affected; but we have also seen the knee and elbow tubercular. The process is exactly the same as in those who are not lepers. Chronic trophic joint affections are by no means so rare as was formerly believed. Prof. H. Heiberg has (*loc. cit.*) drawn attention to this, and has described a foot which resembles that described by Charcot as *pied tabétique*. According to Heiberg a characteristic of these leprous tropho-neurotic joint affections is swelling and laxness of the capsule of the joint, a wearing away and atrophy of the ends of the bones, or *periostitis ossificans*, and hypertrophy of the ends of the bones, which is especially seen in the tarsal and metatarsal joints. We have been able to confirm these results of Heiberg's, and have also seen in such an ankle, growth of the synovial membrane with villous projections; the capsule of the ankle joint was loose and lax, the talus smooth and oblique, the cartilage worn away; and marked outward subluxation of the foot was present. Other older spirit preparations showed changes in the joint capsule, which was

flabby and loose or thickened, and further, slight irregular thickening of the synovial membrane, and thickening of the ends of the bones.

We have also in some cases examined the tendon sheaths; but never, even when contraction had existed for a long time did we find any anatomical changes, which pointed to a tendo-vaginitis. Leloir and Wolff have noted this clinically, but we have been unable to confirm their observation.

The pemphigoid bullæ we have repeatedly examined, and never found lepra bacilli in their contents; both microscopically and on culture we have found only pyogenic cocci, usually the staphylococcus aureus. Müller found (according to Neisser, *Virchow's Archiv*, Bd. 103) lepra bacilli in the contents of a pemphigoid bulla. This was probably a mere accident. For other morbid changes found in maculo-anæsthetic leprosy the reader is referred to TABLE I, page 128.

Maculo-anæsthetic leprosy is therefore characterized by an infection of the skin and nerves directly caused by the lepra bacillus, and by secondary tropho-neurotic affections of the muscles, bones, and joints, the skin and organa sensus.

As is clear from the description of the two forms, the leprosy bacillus is found in the leprous products in both, though in much greater quantity in the nodular than in the maculo-

anæsthetic form. The course of the two differs; in that in the nodular form eruptions constantly recur, and thus the affected areas are much more numerous than in the maculo-anæsthetic. Whether the liver, spleen, and testicle are attacked in the latter form we cannot as yet say with certainty. In one case of maculo-anæsthetic leprosy, we noted an affection of the throat exactly corresponding to that constantly present in the nodular form, and in another we found the inguinal glands affected with leprosy in a manner similar to that in the nodular form. In the maculo-anæsthetic form eruptions are also present, but they are by no means so frequent or so severe as in the other. Both forms may recover. As we have frequently noted in the description of nodular leprosy, the bacilli in the leprous products break up into granules which finally disappear, and there remains of the leprous products only a scar in which nothing leprous can be recognised. Occasionally this takes place in all the affected parts, and there remains only a widespread anæsthesia, the result of the nerve affections; and in the maculo-anæsthetic form this is the regular termination of the disease. In both cases the leprosy is completely healed.

We are thus enabled to see how complete is the parallel between the two forms. The course of the

disease, especially the eruption, gives to it evidently the character of an *infectious disease*. In the nodular form, where the bacilli are present in millions or milliards, the eruptions or auto-infections are frequent ; in the maculo-anæsthetic form, where their number is comparatively insignificant the eruptions are rare.

Does this difference between the two forms depend on a difference in the virulence of the bacilli? This readily suggests itself. But if so, this virulence is capable of very rapid changes. We have seen a case of maculo-anæsthetic leprosy, which probably arose by inoculation from a very severe case of nodular leprosy, since the patient some years before the outbreak of the disease had for a long time shared the bed of a nodular leper. In this case the virulence of the bacilli must have been at once diminished on their inoculation on another organism. And since it also happens that a maculo-anæsthetic case may on a fresh eruption become nodular, the bacilli must be able by cultivation in the organism to re-acquire their power. Both are possible, but the virulence of the bacilli seems to depend, not so much on any constant character of their own, as on the soil in which they live.

Now it is a remarkable fact that in certain regions in Norway the nodular form predominates ;

in others the maculo-anæsthetic does not indeed predominate, but is present almost as frequently as the nodular. The maculo-anæsthetic cases are more numerous in the eastern districts, where the climate is dry; the nodular in the western, along the coasts where the climate is moist. And in this western division there is a region where the climate is not nearly so moist as in the division generally, and here the proportion of maculo-anæsthetic cases is distinctly higher, as may be seen by referring to TABLE III, page 144.

Sogn lies in Nordre Bergenhus, and is an inland fjord with a rather dry climate. Söndfjord and Nordfjord lie nearer the coast, and have, especially the former, very damp climates.

We have already noted that the leprous nodes are most frequently found on the exposed parts of the skin, and it is quite possible that the form is determined by climatic influences.

As the TABLE shows, males are more affected than the opposite sex, and this too may depend on climatic influences.

It is also possible that the bacilli always possess the same virulence, and that it is solely dependant on the soil in which they live, whether they multiply freely or no. But it is impossible to say anything definite on this, so long as we are unable to cultivate the bacillus, and so long as we can only refer to the conditions in Norway; and

nowhere else have we such definite statistics of the disease and its form as to justify us in drawing any conclusions.

We must, therefore, for the present leave in suspense this most important and interesting question of the virulence of the Lepra bacillus, since we possess no experimental proof of any attenuation.

Chapter VI.

DIAGNOSIS AND PROGNOSIS.

DIAGNOSIS.—In view of the description which we have given of the two forms of the disease, the diagnosis is usually accompanied by little difficulty. We have, however, noted above how a case of tubercular Leprosy, with subcutaneous nodules only, was overlooked by a doctor well acquainted with the disease; and we have occasionally seen, in the country, people described by the doctors as leprous who were not so. And, on the other hand, we ourselves were once in doubt as to the diagnosis in a tuberous case, since all the nodules were exceptionally small, and presented no characteristic appearance. But the doubt was readily dispelled by the excision of a nodule and the recognition of the bacillus. In the diagnosis of the maculo-anæsthetic cases, one is more frequently in doubt, since the maculæ have not always a characteristic appearance; sometimes they closely resemble psoriasis, and in such cases the excision and microscopical examination of a portion might clear away doubt. This we have never needed to do, since the swelling of the

lymphatic glands, or a thorough investigation of the sense of touch, have always been sufficient to establish a diagnosis. Even in comparatively recent cases there may almost always be detected some loss of sensation in the fingers and toes ; sometimes it is first evident on the wrists or back of the feet. For this investigation one must either use callipers, or very slight stroking, since deeper *pressure* can be at once perceived. As a rule, the maculæ themselves are somewhat anæsthetic. We recollect once seeing a syphilitic eruption exactly resembling the leprous maculæ, but here the history cleared up the diagnosis.

Maculo-anæsthetic Leprosy may in its later stages be confounded with syringo-myelia, as Charcot has already noted in giving the points of distinction between the two conditions. If the maculæ are no longer present, careful investigation will often enable one to recognise their previous presence by finding areas of skin, especially on the upper arms, the back, the thighs and calves, which are somewhat paler than the surrounding skin, and in which sensation is somewhat blunted. We have thus frequently recognised the previous presence of maculæ in patients who themselves knew nothing of them. Zambaco Pasha has stated that certainly many of the cases described in France as syringo-myelia and Morvan's disease are cases of Leprosy ; that

Leprosy in this form still exists in Brittany; and further, that he has there found some cases of nodular Leprosy. It is remarkable that in these last cases, where the proof would have been so easy, he has not demonstrated the Lepra bacillus. From the drawings which he gives in the *Annales de Dermatol. et de Syphil.* (T. III., Nr. 12), some of the cases can scarcely be regarded as Leprosy, since on the hands with mutilated fingers, no muscular atrophy can be noted; but in others there is distinct atrophy, and these may very well be leprous, the more as Pitres has published in the *Gaz. des hôp.* 1892, a case diagnosed as syringomyelia in which Lepra bacilli were demonstrated in an excised portion of the ulnar nerve. It is unfortunate that Zambaco Pasha did not demonstrate the remains of previous maculæ, which would probably have been possible in some cases, were they really cases of Leprosy. According to the rich experience of Dr. Danielssen and our own, it must be admitted that a skin eruption is never absent in true cases of Leprosy. With multiple neuritis from some other cause, it is, with a good history and careful examination, not possible to confuse Leprosy; and the same is true of progressive spinal muscular atrophy, where there is no disturbance of sensation.

PROGNOSIS.—The prognosis is very different in the two forms. As we have already

stated, both forms may recover, since all leprous products may disappear without any fresh ones appearing. *In nodular cases this is a very rare exception, while it is the rule in the maculo-anæsthetic.* Recurrent outbreaks are almost invariable in nodular cases, and in them, too, nephritis is an almost constant occurrence. Patients rarely live more than eight or nine years after the definite outbreak of the disease. As already remarked, we cannot state that Leprosy of itself is responsible for the end ; we are rather inclined to regard the nephritis and other complications as the direct cause of death. The patients usually die long before the disease has run its course. But in the maculo-anæsthetic form the cure of the Leprosy is almost invariably the result. What remains, however, after the cure of the leprosy, is very different. We have occasionally a complete subject with vigour and good health, but usually only a miserable rudiment of a human being, with more or less paralysed and deformed hands and feet, with unclosable eyes, of which the lower part of the cornea is opaque, and from which the tears run down over the cheeks, and with paralysed facial muscles unable to close the mouth, so that the saliva constantly dribbles from it. Such cases may, however, live long and reach great ages, if under such circumstances this can be looked upon as any advantage. They die usually from some intercurrent disease.

Chapter VII.

ETIOLOGY.

THERE is hardly anything on earth, or between it and heaven, which has not been regarded as the cause of Leprosy ; and this is but natural, since the less one knows, the more actively does his imagination work. And since all that was known of Leprosy was that it was a loathsome disease, search was made everywhere for a cause. We will not linger over the older literature of Leprosy. That may be found fully dealt with in Danielssen and Boeck's *Traité de la Spedalskhed* and in Hirsch's *Geographical Pathology*.

Only after the work of Danielssen and Boeck can one say that Leprosy entered the ranks of the scientifically investigated diseases. At that time, in 1840, when they commenced their investigations, Humoral Pathology held the field. Most diseases were ascribed to changes in the blood, and they therefore endeavoured to establish that there was in lepers a change in the blood which they regarded as the cause of the disease symptoms, especially the node formation. These changes in the blood they believed were caused by unfavourable conditions of living, and as they

were not able to find any convincing evidence of the power of infection of the disease but several of its limitations to certain families, they drew the conclusion that Lepra, as they called it, might appear spontaneously, that is to say, that the sanguineous dyscrasia which led to leprosy could be developed under unfavourable conditions of life, but that it was in most cases hereditary. It must, however, be noted that Danielssen always regarded Leprosy as a specific disease, described it as such, and sought for a specific cause, and the fact that he did not find it must be ascribed to the circumstance that microscopical technique and microscopical aids, especially the immersion lens, were at that time either insufficiently developed, or not yet discovered. The teaching of Danielssen and Boeck was everywhere adopted, especially their view of the heredity of the disease. The fish diet and damp cold theories are only attempts to explain the so-called spontaneous development of the disease, and they are founded on the fact that Leprosy is chiefly present in littoral districts and on islands.

Of other Norwegian investigators, the late Dr. Hjorth held the view that Leprosy could not be ascribed to a specific cause, and that it was certainly not hereditary. Dr. Holmsen regarded it as a specific miasmatic and non-hereditary disease, and finally Prof. Lochmann stated that it was

specific, contagious, and hereditary. While Danielssen and Boeck always required a leprous ancestor in order to recognise a case as hereditary, and when this was not forthcoming, found in the presence of the disease in other branches of the family, proof of its heredity, Biedenkap, as he was unable in many of his cases to determine the existence of leprous ancestors, widened the definition of heredity by assuming that unfavourable conditions of life might produce in the organism conditions which became hereditary, and showed themselves in later generations as leprosy. In the year 1869, Dr. Drognat-Landré published a book with the title, *De la contagion seule cause de la propagation de la lépre*, in which he sought to prove that heredity had nothing to do with the spread of Leprosy. That is, according to our view, the right standpoint, as we shall endeavour to demonstrate.

As is seen from the above short summary of the views of Norwegian investigators, some maintain the non-specific origin and heredity of the disease; one only, the non-specific origin; one a specific cause and no heredity; and finally, one a specific cause, contagiousness and heredity.

It is rather remarkable that supporters both of the specific and the non-specific origin of the disease should regard it as hereditary. It apparently struck none of them that possibly the

specificity of a disease, that is, its development through the action of a poison, might be incompatible with heredity. Since the discovery of the Lepra bacillus and its recognition in all leprous products, it is now everywhere admitted that it is the cause of the disease, and it would therefore be superfluous to indicate which of all the symptoms of the disease point to its specific nature. All this was shown in a communication made by one of us to the Copenhagen Congress in 1884. We start then from the assumption that Leprosy is a disease caused by the Lepra bacillus, although it is as yet not strictly scientifically proved, since inoculation on man and animals has not been definitely successful.

The question as to heredity now is, Can the lepra bacillus be conveyed by heredity. This is Baumgarten's view ; he holds that both Tuberculosis and Leprosy are thus spread, that the bacilli of both diseases may be transferred to the children and there remain dormant, but that they can thence be conveyed to another generation, and from it to a fourth, fifth, etc. generation, and then in the third, fourth, etc. generation become once more active and cause the disease. We see at once that this is only a modification of Biedenkap's heredity, a peculiarity of the organism which finally becomes evident as Leprosy. In place of his undiscovered peculiarity, we have undiscovered

latent bacilli. Baumgarten's view is therefore only a hypothesis for the explanation of the origin of the two diseases. The hypothesis may be tested from two points of view: first, we may sift it theoretically; and secondly, we may investigate whether it can explain the distribution of the disease.

We must first endeavour to make clear *what heredity is.* As a matter of fact we do not know; we are familiar only with a series of phenomena which we call heredity, just as we have a series of phenomena which we ascribe to the force of gravity, without knowing what gravity or its force actually is. If we consider only the phenomena of heredity, which are nowhere so completely and clearly put together as in Darwin's works, we find that he presents so-called laws of heredity, that is, he has noted the most frequent phenomena of heredity, and thence deduced a law. If the phenomena in the conveyance of a disease to one's descendants are to be called heredity, they must correspond with the rest of the phenomena of heredity. And looked at thus, we know of no specific disease which can be called hereditary. The conditions which are hereditary are all anatomical and physiological peculiarities of the organism. A bacillus which is living in the organism cannot be regarded as one of its anatomical or physiological peculiarities; it is a parasite. Now it is beyond doubt that parasites

may be conveyed from parents to children. Such are the *Achorion Schönleini*, and the *Acarus Scabiei*. But this is no hereditary communication, it is simply a present from the parent to his child. But, it is objected, if the parasite is conveyed through the organs of generation during copulation, then it is no longer a present or an inoculation, it becomes hereditary. This appears to us a remarkable argument, that conveyance by means of the organs of generation can change the nature of the parasite and convert it into an anatomical constituent of the organism of parent or child. A parasite remains always a parasite, and since its conveyance from one adult to another is called infection, we cannot comprehend why its conveyance to an ovum or a fœtus should be indicated by another name. Were Baumgarten's hypothesis correct, it should certainly be called a hypothesis of latent infection, and not a hypothesis of heredity. We said above that we knew of no specific disease which was hereditary. To this it will naturally be objected that syphilis is a typically hereditary disease. But we reply that syphilis is a disease communicable to children, but that it is not hereditary, and in order to maintain this statement we only need to place in parallel the phenomena of the conveyance of hereditary peculiarities and those of the communication of syphilis to children, in order

to make it perfectly clear how different the two methods are.

Conveyance of Hereditary Peculiarities.	Conveyance of Syphilis to Children.
1.—The hereditary peculiarity is usually limited to one sex, so that the male communicates his peculiarities to his male descendants, and the female hers to the female.	Not the case in syphilitic children.
2.—Very often, possibly always, the appearance of the hereditary peculiarity is limited to a definite age.	In the communication of syphilis to children this is unknown.
3.—Atavismus, or the overleaping of one or several generations of the heredity is very frequent.	Never known.

Anyone who will maintain that these two forms of conveyance are the same, and both hereditary, must evidently sacrifice facts.

We hold then, that a specific disease may be conveyed to the children, but that it is never hereditary ; the communication is by infection.

And since we regard leprosy as a specific disease we hold that it cannot be hereditary. There remains, however, the further question whether it can be conveyed to descendants by latent germinative infection. This cannot *a priori* be denied, although we have no right to assume it from our knowledge of the lepra bacillus and of

the occurrence of the disease. We have indeed sought above to point out the possibility that the lepra bacillus is attenuated in the maculo-anæsthetic form of the disease ; but we know of no phenomenon which would allow us to assume that the bacillus could occasionally become quite innocuous, and call forth *no* symptoms of disease.

All this, however, proves nothing against the hypothesis ; and it is always a dangerous thing to use a simple absence of knowledge either to contradict or to found a hypothesis.

But we think we can supply an almost incontrovertible proof that Baumgarten's hypothesis is wrong. It is well known that the Belgian Father Damien became a leper in the Sandwich islands. If the Father was of pure Belgian ancestry, and his disease was caused by latent hereditary bacilli, then these bacilli must have been at least several hundred years old, unless one assumes that one of his nearer ancestors had had connection with a leper, and that in this way the Father had acquired his bacilli. Against this is the explanation that the Father who tended the lepers on Molokai, with self-sacrificing love, was, through some want of care or caution, infected as he went in and out among the lepers. The choice between the two explanations does not appear to us a difficult one.

The view of the non-communication of leprosy

by latent bacilli is further strengthened by the fact that there are places in Norway where many descendants of lepers live without one single one of them becoming leprous, as for example, in the town of Bergen where the descendants of lepers may certainly be numbered by thousands; and further, we have demonstrated by our investigations in North America, that of the numerous descendants of Norwegian lepers there, not one has developed the disease. But since about one hundred and seventy leprous Norwegians have emigrated to America, it may possibly be that the disease is spread by infection. There are indeed cases in America which have possibly arisen from infection, but they are not sufficiently definite to serve as arguments for its contagion. But even if leprosy be a contagious disease, one can easily understand how it should spread little, or not at all, in North America, when one compares the social condition and especially the cleanliness there with that in Norway, and probably especially with that of the districts in which leprosy is most prevalent. In North America the dwelling houses are roomy, so that the lepers whom we saw there had usually their own room, or at least their own bed; and everywhere, even among the Norwegians, great cleanliness is observed. And this is, according to our view, sufficient isolation

in order, in most cases, to prevent the spread of the disease.

That leprosy is really contagious is primarily evident from its nature as a bacillary disease. No one has been able to demonstrate the presence of the bacillus outside the human body, so that we may abandon the idea of a miasmatic origin.

Unfortunately, all attempts to inoculate animals have failed. The now old experiments of Neisser and Damsch, as well as our own, we may pass over. We dealt with them in our Copenhagen communication. Since then Mèlcher and Ortmann believe that they have communicated the disease to rabbits. Dr. Ortmann has kindly sent us preparations from the infected rabbits, and on close examination of them we regret to say that we lost our faith in the leprous nature of this affection of rabbits. We found both caseous degeneration and myelo-plaques in the preparation, which, as we have noted, we have never found in leprosy. At the same time the affection does not look exactly like tubercle, and it is possible that in rabbits leprosy appears otherwise than in man. But we may note that Veterinary Surgeon Nielsen has, here in Bergen, observed a disease in mice, which shows a close resemblance to Ortmann's rabbit leprosy. Inoculated on a rabbit, the disease appeared with new growths in the cœcum, just

like Ortmann's rabbit leprosy. These new growths had certainly more resemblance to tuberculosis; but there were in them, at many places around the vessels, cells, crammed full of bacilli. Nielsen's investigations are not yet concluded, but it is possible that the disease is one of animals as yet unknown, which Melcher and Ortmann have by chance conveyed to their rabbits. All the inoculations of leprosy on rabbits which Dr. P. F. Holst made in the laboratory of the Lungegaards Hospital were unsuccessful; not one of the infected animals became leprous.

Although, as we have stated above, the lepra bacillus has never been found outside the human body, this might possibly be dependent on insufficient search, and it might be possible that the old view at present maintained by Hutchinson is the right one, viz., that leprosy is caused by the eating of putrifying fish, or that the contention of Holmsen that leprosy is a miasmatic disease, is correct.

Against Hutchinson's hypothesis there is in the first place the fact that we have never succeeded in cultivating the bacillus, which, if the bacillus lived as a saprophyte on decaying fish, would be a very simple matter. And there are, secondly, places where the inhabitants certainly and frequently enjoy decaying fish without the disease appearing. And thirdly, there are many places

authoritatively indicated where leprosy is present, and where no fish is ever eaten. For his hypothesis of the miasmatic origin, Holmsen can only bring forward the fact that the disease is often limited to certain districts. This is certainly correct, but this endemic appearance of leprosy may be as readily explained by infection, while the localities affected do not give the slightest support to the assumption of a miasma. Such areas are found here in Norway, both on the bare cliffs, on the coast, in the valleys, and on the mountains.

There is, therefore, no other course open to us but to assume the infectiousness of the disease, and thus the spread of leprosy is readily understood; while by the assumption of heredity, or Baumgarten's latent germinative infection, it remains absolutely inexplicable. These two last causes are to our thinking absolutely proved to be non-existent by the case of Father Damien; by the results of our investigations in North America; and by the diminution of the disease in the descendants of lepers in the Norwegian towns.

But *direct proofs* of its contagiousness may also be obtained. Such are given by Drognat-Landré in his book, and also by many other observers. Norway can supply many proofs; but against these it can always be urged that it is impossible to exclude the possibility of inheritance on account of the wide-spread nature of the

disease. But we think we can supply from Norway a still better proof in the shape of the gradual diminution of the disease during the last thirty-five to forty years.

Up to 1856 leprosy probably increased in Norway; we cannot speak more definitely, as previous to that year there was no exact or sufficient enumeration of the lepers. But we have grounds for believing that we have obtained, by means of the yearly census begun in 1856, a pretty exact knowledge of the number of new cases in the years 1851-55, and this shows that the number is considerable, and almost exactly corresponds with the number of new cases in the next five years, 1856-60. This, we think, indicates that the total number of lepers in the two quinquenniums was pretty much the same. Now we know that there were in Norway in 1856 over 2800 lepers. The number was estimated in 1836 at 659, and in 1845 at 1122. According to this estimate a considerable increase had taken place. We can, however, with certainty say that the numbers for 1836 and 1845 are too low. In the first place, the enumeration was not undertaken by medical men, and secondly, even now, there are many lepers overlooked at every enumeration, or, to speak more correctly, they are not discovered because the patients conceal their condition. But that the number of those overlooked in the

years 1836 and 1845 can have been so great as the difference between the numbers for those years and that for 1856 is scarcely credible, and it therefore appears probable that the number of lepers in Norway increased during the first half of the century.

In the year 1856 the first Leper Asylum was opened in Bergen. Previously to this we had in Bergen the St. Georg and Lungegaard's Hospitals, which together served for 200 patients. In Molde there was also a small hospital for lepers, so that altogether in the year 1856 there were about 235 lepers in hospital. In 1861 were opened two new asylums, one in Molde, the other in Trondhjem (Drontheim), and as is seen in TABLE IV (p. 145), since that time a large number of lepers have been admitted to these institutions.

We may regard the numbers in this TABLE up to 1885 as accurate; for the later years corrections will have to be made from the later enumerations, which may detect older, concealed cases. But these can only affect the figures to a limited degree.

If we consider the TABLE closely, we see that in the first quinquennium (1856-60) the total number of lepers is 76 less, while those in their own homes are 380 less; during this period 585 lepers were admitted to the asylums. The number of lepers as a whole, then, was not much reduced, but at

the end of the period there were 380 lepers fewer at home, or, in other words, there were among the people 380 fewer sources of infection, and to this we ascribe it that while the number of new cases was 1,148 in the years 1856-60, it fell in the years 1861-65 to 1,028. The mortality of the year 1856 we do not know; in the four following years 981 died—668 at home, in the asylums 313. If we assume that there died at home as many in 1856 as in 1857, viz., 230, then the number of deaths at home during the quinquennium would have amounted to 898, and the whole mortality, adding the 313 who died in the asylums, would have been 1,211—only 109 more than the new cases. But one must not so reckon. There died, especially in the early days, a much larger proportion in the asylums than outside; and it is evident, secondly, when one observes the figures in a district from which at the commencement only very few cases were sent to the asylum, that the new cases are much more numerous than the deaths. In Nordmoere, for example, the number of new cases from 1856-60, was 81; that of deaths, 46; only 14 were sent to the asylums, and the disease increased during the quinquennium, the cases rising from 105 to 119. One finds the same thing in Soendmoere—new cases 104, deaths 42, sent to asylums 28; number of cases in 1856, 178; in 1860, 195. In these two districts, then, the disease was evidently

on the increase, and this would probably have been the case throughout the country, had many cases not been removed from their homes to the asylums; as, for example, in Soendfjord. Here there were, in 1856-60, 214 new cases, 116 deaths, 211 sent to the asylums; number of cases 1856, 431; 1860, 306. If we examine in this way the numbers in the different districts, we find everywhere that decrease of the disease depends on the numbers isolated in the asylums. Where isolation was insufficient or absent, there was no decrease, but either the numbers increased or remained stationary; where, on the contrary, isolation was thorough, the decrease was invariable. This can only be explained in one way, viz., that isolation is the cause of the decrease, and isolation can only have effected improvement by removing from the homes of the people the sources of infection. Further, during the next five years, the number of new cases in those districts where isolation was good continued to sink; where there was none, or it was insufficient, the numbers either rose or remained almost stationary. We will once more compare Nordmoere with Soendfjord. In Nordmoere, in 1856-60, 81 new cases, 14 sent to the asylum; 1861-65, 88 new cases. In Soendfjord, 1856-60, 214 new cases, 211 sent into asylums; 1861-65, 146 new cases.

We consider it superfluous to point out further

how the isolation of the patients has caused the decrease of Leprosy in Norway. It is not possible to explain the action of isolation by the elimination of heredity; the time is too short for that. The only one possible solution is that which we have given, and therefore we regard this decrease of Leprosy in Norway following on isolation as the best proof of the contagiousness of Leprosy. Leprosy is, then, according to our view, a contagious disease, and only contagious, not hereditary.

How Leprosy is "caught," we do not know, but we think it is probably by inoculation; and the nodular form must be more dangerous than the maculo-anæsthetic. This last statement seems to be confirmed by the fact, that in Sogn, where 56·6 per cent. of the cases are nodular and 43·4 per cent. maculo-anæsthetic, the increase varies between 8· and 10·8 per cent., while in Soendfjord, with 72·6 per cent. nodular, and 27·4 per cent. maculo-anæsthetic, it is between 14·4 per cent. and 19·5 per cent. In the nodular form there are incomparably more bacilli than in the maculo-anæsthetic, and in the latter there is no discharge containing bacilli, which in the former is almost always present. It is not improbable that Leprosy may be conveyed by the clothes. We know of one case in which a young man became affected one year after he had worn a pair of old drawers

given him by a leper. The same thing happened to another young man who wore several pairs of his leprous father's stockings.

Although we are not acquainted with the spores of the Lepra bacillus, it is quite conceivable that the bacilli are spore bearing. Unfortunately, we know of no method of determining whether the bacilli are alive or dead, and therefore Arning's observation of the bacilli in the fæces does not decide the question as to whether the bacilli can live for any time outside the body, even admitting that the bacilli which Arning found were actually Lepra bacilli.

After completing this work I received "The Recrudescence of Leprosy and its Causation," by William Tebb. The author seeks to prove that leprosy is everywhere on the increase as the result of the introduction of vaccination. The book as a whole is directed against vaccination as dangerous. Distinct proofs for his contention that leprosy may be conveyed by vaccination from arm to arm, the author, to our thinking, does not supply. Since Dr. Arning found lepra-bacilli in the contents of vaccine vesicles in lepers, the possibility of the communication in this way can scarcely be denied. But that it can be frequent, I cannot possibly believe. In Norway, vaccination has been compulsory during all those years in which leprosy has steadily diminished. In 1891 I

put the question to all those doctors in Norway who had anything to do with leprosy, whether they had ever met in their practice with a case which could be ascribed to vaccination. Not a single one had observed such a case. And yet, here in Norway, lymph must often be taken from the children of leprous families. But since leprosy is very rare in children, it is evident that leprosy cannot be conveyed in this way. That vaccine vesicles in the non-leprous members of leprous families contain lepra-bacilli is incredible.

Chapter VIII.

TREATMENT.

SINCE many cases of Leprosy terminate in cure by the disintegration and elimination of the bacilli, one might imagine that it would be a tolerably easy task to find a suitable treatment for the disease. But this is far from being the case. Treatment of Leprosy has been carried out from time immemorial. In the Bible there is little concerning any treatment which was regularly applied in Leprosy; the disease being apparently regarded as beyond human power. Later, all possible and, we may say, impossible remedies, such as the teeth of elephants, the flesh of crocodiles and serpents, the fat of panthers, lions and bears, and so on, were applied. In mediæval times, the same class of remedies was used along with religious incantations.

In the eighteenth century, Schilling tells us he treated leprosy with success. For the first three months he ordered a rather sparing diet, consisting of bread, vegetables and soup. The real treatment began with purgatives, "not mineral ones, because these are dangerous for lepers, and often produce dangerous diarrhœa," and was followed by warm

baths, "with circumspection, when the disease is far advanced, because they produce palpitation of the heart, convulsions and fainting fits." In addition to advising frequent exercise in the open air, Schilling regarded it as important to dilute the diseased humours by large quantities of purifying fluids, of which he used first emollient decoctions, and later, powerful sudorific ones. As mild ones he used barley water, infusions of herbs, Agrimony, Hedera terrestris, Fumaria, Veronica, etc., to which were sometimes added other softening and purgative remedies, such as Malva, Parietaria, Senna and Rhubarb.

Of these the patients took, for six weeks, 3 to 4 litres daily. He then gave powerful resolvents and sudorifics, as Saponaria, Zedoaria, Sassafras, Juniper, Fol. Scolopendrii, herb. Cardui benedicti. Pareira brava, etc. The more the patient could take, the more rapid and complete, according to Schilling, was the cure. Rich food and good wine might be given. During the treatment the patient had to guard himself from cold air. After three months the patient was bled, as much blood being taken as his strength would allow. The external remedies which were used when there were putrid ulcerations, and when fingers and toes commenced to fall off, were tincture of aloes, myrrh, and succini, which were dropped on lint and applied twice a day. Both the pharmaceutical

and the dietetic remedies were to be persevered with until definite signs of cure were manifest, and the treatment was to be continued for many months after apparent recovery. Many years ago this method of treatment was carried out at the Lungegaard's hospital, but without success.

We shall next mention all the specific remedies which have been recommended and have acquired any reputation as effective.

Madar (Mudar) is one of the oldest. It is got from the Indian plant, Caloptris gigantea (*Asclepias gigantea*). Only the powdered bark of the root was used. Some of it was sent from India to the Lungegaard's hospital, and was given in large doses to many lepers. The effect was absolutely *nil;* one might just as well have given them flour.

Dr. George Watt enumerates the following plants of which the oils have been used in India in leprosy:—(1) Albizzea Libbek, (2) Anacardium occidentale, (3) Gynometra ramiflora, (4) Dipterocarpus turbinatus, (5) Gynocardia odorata, (6) Hydnocarpus Wightoni, (7) Hydnocarpus venenata, (8) Pongania glabra, (9) Psoralea corylifolia, (10) Sunocarpus anacardium, (11) Arachis hypogæa. Of these, only a few merit more particular mention; the others have been mostly merely popular remedies.

Cashew-nut Oil, from Anacardium occidentale,

Linn., Cassuvium pomiferum, Lamk, a large tree very common in the West Indies. The oil is found in the pericarp, and is extracted by ether, which, after being evaporated in open vessels, leaves a thick, brownish black oil—the Cashew-nut oil. This is the oil with which the French physician, Dr. Beauperthuy, in Cumana, Venezuela, claimed to have cured leprosy. An English physician, Dr. Bakewell, who had investigated the treatment of Dr. Beauperthuy, sent a report to both houses of parliament on the beneficial effects of the treatment, and it thus attracted much notice. Dr. Beauperthuy's method of treatment was the following: good nourishing diet, good hygienic surroundings, frequent warm baths followed by the inunction of olive oil, and internally $\frac{1}{16}$ to $\frac{1}{20}$ of a grain of bichloride of mercury twice daily, or, when this was contra-indicated, 10 to 20 grs. of carbonate of soda. As external remedies, which Beauperthuy regarded as the most important, he applied different liniments, such as tincture of iodine, to which were added potash lye, olive oil, and balsam of copaiba mixed with yolk of eggs. These liniments he principally applied where herpetic or other eruptions complicated the leprosy, and to the specific eruptions he applied solutions of nitrate of silver or sulphate of copper, but especially Cashew-nut oil. In all this there is nothing new except the oil; all the other

remedies have been long, and still are occasionally, used. In the Lungegaard's hospital, the oil was tried on five patients exactly according to the directions of Dr. Beauperthuy, and after a trial of several months, the results were anything but good. The oil induced irritation, redness, swelling and vesiculation; the leprous tubers and patches remained unaltered, and in one case a leprous eruption developed, probably produced by the irritation of the oil. In Trinidad, too, the same results of the application of the oil were seen, and Dr. Beauperthuy's treatment has been given up.

Even before Dr. Beauperthuy's remedy had lost its reputation, a new specific remedy appeared in the East Indies, viz., *Gurjun oil*, introduced by Surgeon-Major Dougall, of the Andaman Islands. The oil is procured from several species of Dipterocarpus, principally D. lævis, D. tuberatus, and D. trinervus. Dr. Dougall's method of treatment was the following: good nourishment, fresh air, and a mixture of gurjun oil and lime water internally and externally. For internal use he gave a mixture of equal parts of oil and lime water, which forms a tolerably thick emulsion, 15 grains morning and evening. Externally, he used an ointment of oil 1 part, and lime water 3 parts. With this the patients rubbed the whole body for two hours both forenoon and afternoon. The body was thus covered with a sticky layer, to which dust and dirt

adhered. To remove this, the patients rubbed themselves every morning with dry earth, and afterwards took a bath in running water, before again applying the oil. The prolonged rubbing he considered not only beneficial to the skin, but useful as a gymnastic exercise. Of twenty-four lepers whom he treated in this way for six months, all, without exception, improved; all ulcerations healed without again breaking down; and, what is most remarkable, the anæsthesia almost or completely disappeared.

According to his description of the patients, some of them evidently had syphilis, some chronic eczema, and some psoriasis. Their ulcerations had been so neglected that flies laid eggs in them, and it is little wonder that they healed under the cleanliness which Dr. Dougall induced. That old anæsthesia should disappear within six months, is, to any one who knows leprosy, absolutely incredible.

In the summer of 1887 the Lungegaard's hospital got a sample of the oil, and nine male lepers underwent Dr. Dougall's treatment, the only difference being that they took a warm bath instead of a bath in running water, which Dr. Dougall probably ordered because he had no bath-rooms at his disposal. Every morning and evening the patients took 15 grains of the mixture of equal parts of oil and lime water. In the fore-

noon, from 9 till 11, and in the evening from 5 till 7, they rubbed each other in a room at a temperature of 26 to 28° R., with oil 1 part and lime water 3 parts. In the morning they rubbed themselves with dry earth, and took a warm bath before re-applying the oil. The treatment led to no results. In some of the patients the disease advanced very little, but, nevertheless, the gurjun oil had no effect. As leprosy, so far as we know, is the same disease in the East Indies as in Norway, it was surprising that the gurjun oil should cure it in the one place and not in the other. Later trials of the treatment in India have had the same negative results as in Norway.

Chaulmoogra, which the medical department of Madras has used with success, is the oil pressed from the seeds of Gynocardia odorata, Lindl. Hydrocarpus odoratus, Lindl. The oil is given internally (2 grs. in an ounce of milk) twice daily, and externally, there is rubbed in a mixture of oil 1 part, and olive oil 16 parts, followed some hours after by a bath. We are told that the progress of the disease is stopped by a persevering use of the oil. The skin becomes smoother and more elastic, the patient becomes more energetic, the discolorations disappear, and so too does the anæsthesia, either partly or completely. Ulcerations heal, but promptly break down again. Besides the treatment, a generous diet is given, especially

vegetables, milk and meat ; spices and spirits are not allowed. Dr. Arjoon says that the tuberous form heals more easily than the mixed leprosy, and that anæsthetic leprosy is the most obstinate. When the disease is inherited there is no hope of a cure, and it is only in early cases that a cure can be expected. Further, he thinks that the permanence of the cure is doubtful.

In the Lungegaard's hospital three tuberous and two anæsthetic patients were treated with chaulmoogra oil. The treatment was continued from eight months to a year, but the results were, as with the other remedies, *nil.*

Father Etienne sent to the Lungegaard's Hospital from Port of Spain, Trinidad, a quantity of pills containing a vegetable, Hoang-nan, which he had received from some missionaries in Ting-King. He had used the pills for three years in leprosy with surprisingly good results. In several patients all the external symptoms of the disease disappeared, and he had good hopes of their complete cure. His report seeming to guarantee the remedy, it was given a trial in the Lungegaard's Hospital. After prolonged use it proved to be absolutely useless, and, since no more has been heard from him, Father Etienne has probably been disappointed with his later results.

Father Damien also received from Ting-King a supply of pills for the cure of leprosy, which

were, no doubt, of the same nature. He found them to consist of alum. sulph., pts. 1·5, Realgar 2·5, and Hoang-nan 2·5.

Hoang-nan belongs to the *Euphorbiaceæ;* the cortex contains a powerful poison which is the active remedy. At first Father Damien believed the remedy to be of some benefit "to us poor lepers"—he was then a leper—but further experience showed him that the remedy was, like so many others, unsatisfactory.

The last remedy to be mentioned is one which once attracted much notice, and on which the French academy allowed Dr. Gibert to write a report. The remedy is *Assacou* or *Ussacou*, Brazilian names of the tree *Hura Braziliensis*, Martin, of the family *Euphorbiaceæ*. It is considered very poisonous.

Several physicians in the West Indies have tried it, and amongst them Dr. Maldur, who treated four lepers in Santa-Caza da Misericordia, with, he believed, great benefit; other trials, however, failed, and the remedy has been laid aside.

The foregoing reports of the results of the treatment of leprosy with different specific remedies, are taken from the experience of the late Dr. Danielssen, who spent half a century trying to cure leprosy, and we shall now give some of the various methods of treatment he used.

Early in the development of bacteriological research, Dr. Danielssen already suspected the bacterial nature of the disease, and began to use germicides.

Carbolic acid was given in solution, 8 grains to 8 ounces, 1 tablespoonful four times daily, and he went so far as to give 20 grains to 8 ounces in the same way. Externally, he applied carbolic acid as an ointment or a lotion. It was used by fifty-three lepers from three to eighteen months, but had no effect on the disease.

Creasote was used in 1838 by the late Dr. Hjort, and later by Danielssen, without any good effect. Prof. Langerhans of Madeira, told Dr. Danielssen that he had seen several lepers on Teneriffe, whom Dr. Perez, at his suggestion, treated with creasote in increasing doses, with good effect, and he therefore asked Dr. Danielssen to try it once more. Consequently, creasote in pills (0·025 gr. in each pill) was administered to five tuberous lepers, in an early stage of the disease. They took the pills for six months without any effect on their leprosy. Two of them took the pills for fifteen months, and as many as 20 pills a day. The pills did neither good nor harm; their influence on leprosy was *nil.*

In the early years of the Lungegaard's hospital (1849-50) glacial phosphoric acid was largely used without benefit.

Phosphorus was given in doses of 2 to 3 milligrammes daily. After some months it was given up because it caused indisposition and destroyed the appetite, while the leprosy remained unaltered.

Arsenic has been used by many physicians in the treatment of leprosy. Dr. Danielssen tried it in the form of Fowler's solution, and the so-called Asiatic pills, in gradually increasing doses, but the prolonged use of arsenic, instead of doing good, made the patients worse, causing gastro-enteritis and emaciation. The emaciation caused diminution in the size of the tubers, which has been regarded by many physicians as an improvement; but this is a fallacy, for, when the patient regains his former good condition, the nodules regain their former size.

Ichthyol was tried internally in the form of pills, 10 centigrammes thrice daily, increased up to 2 grammes daily; but no benefit was observed, although it was continued for almost a year.

From Dr. Englemann, in Kreuznach, Dr. Danielssen got a sample of Kreuznach salt, and directions how to use it. The bath was prepared thus: 3 lbs. of common salt, 4 lbs. of Kreuznach salt, 264 litres of water. Temperature 35°C. After the lapse of a week the Kreuznach salt was increased to 6 lbs., after a fortnight to 12 lbs., and after three weeks to 16 lbs. The

patient remained from one-and-a-half to two hours in the bath, and no other medicine was taken. Forty-six baths were used by five lepers, four tuberous, and one anæsthetic. At the same time, a young man with a recent eruption of leprosy was sent to Kreuznach to take the baths under Dr. Englemann's directions. After a year Dr. Danielssen saw him again, when no improvement was to be observed, and the same was the result in the cases treated here.

Mercury in its different combinations has been tried internally and externally, but instead of producing any good effect it has rather made the condition of the patient worse.

Iodine has been used as iodide of potassium, and externally as tincture of iodine and iodine ointment. At the beginning of his studies in leprosy Dr. Danielssen had great confidence in iodine, but he soon learned what a very dangerous remedy it was in this disease. Even small doses of iodine produce new eruptions of leprous tubers or patches, and Dr. Danielssen therefore ultimately used it as a test in cases of apparent cure. When a patient was considered cured, he gave him iodide of potassium, and if no new eruption developed, the cure was considered complete.

Some years ago Dr. Unna, of Hamburg, claimed to have cured three lepers, and Dr.

Danielssen, using Unna's method, cured one. The treatment is the following: Internally, pills of ichthyol in increasing doses; externally, the rubbing of arms and legs morning and evening with an ointment of 10 per cent. pyrogallic acid in lanolin, and the breast, back, neck, and cheeks, with 10 per cent. chrysarobin in lanolin; the covering of the forehead and chin with a plaster consisting of chrysarobin, salicylic acid, and creasote, which is changed every second or third day. This treatment was continued from December 16th, till January 11th; then followed a few days of plain baths, and then the same treatment again. In the Lungegaard's hospital Dr. Unna's treatment was tried by thirteen lepers, five nodular, four anæsthetic, and four mixed. The results of the treatment were not so satisfactory as in Dr. Unna's hands, and there was certainly no question of a cure.

Koch's tuberculin was administered to five anæsthetic, three tuberous, and three mixed cases, as a rule, daily, from January 8th to May 8th. The dose at the commencement was 1 milligramme, and in several cases as much as 320 milligrammes were finally injected. The injections were made, sometimes daily, sometimes at intervals of a few days, according to the degree of reaction which followed the injections. In some cases the injections had to be stopped very soon, because

they produced fresh leprous eruptions; and in one case bacilli were found in the blood. It seemed as if the tuberculin had set the bacilli afloat. We came to the following general conclusions:—(1) Tuberculin administered to lepers produces a general and local reaction, usually forty-six hours after the injection, seldom after twelve hours, and very seldom after two to three days. The local reaction becomes evident later. (2) These reactions do not beneficially influence the leprosy, they rather aggravate the disease by causing fresh eruptions just as iodide does. (3) Tuberculin does not kill the lepra bacillus. (4) Immunity against tuberculin can be attained, but this immunity does not influence the progress of leprosy.

Dr. Carreau, in Guadaloupe, treated a leper with *chlorate of potassium*, he believed with great benefit; he gave the remedy in enormous doses. Dr. Hjort had, already, in 1838-39 tried this remedy without effect. Dr. Beaven Rake has also tried the remedy according to Dr. Carreau's directions, but also without result. Dr. Danielssen, too, tried it, but without any benefit.

During the last few years the following remedies have been tried in the Lungegaard's hospital: Hydroxylamin, Europhen, Naphthol, Salol, Methylene blue, Aristol.

Hydroxylamin forms colourless crystals, easily

soluble in alcohol and glycerine. It is decidedly poisonous, and is, according to some authors, a more powerful reducing agent than chrysarobin or pyrogallic acid; 2 to 5 hydroxylamin to 20 glycerine and 80 alcohol, was painted on the patches of four maculo-anæsthetic lepers. In two of them there developed, after the painting, an erythema, during the persistence of which the painting was discontinued. The painting was continued for two months, and then a 2 per cent. hydroxylamin ointment was applied, but as no amelioration could be noted after four or five months, the remedy was laid aside. In four tuberous patients the painting could only be continued for two or three days, because the spots re-acted severely, grew red and painful, and vesicles formed. The tubers somewhat diminished, but otherwise the condition remained unaltered.

Europhen has some resemblance to iodoform, but gives up its iodine less readily. It is a fine yellow powder, insoluble in water, but soluble in alcohol, ether, chloroform, and oil. A solution in oil was used for hypodermic injections: at first 0·015 europhen was injected, and after a month 0·025. At the end of another month an eruption developed in one of the patients; in the others no effects were evident, and thereupon 0·030 was injected. After three weeks an iodine

eczema developed in three of the patients, and a leprous eruption in another, and consequently no further trials were made. Dr. Julius Goldschmidt of Madeira, has also used this remedy, and considers one of his patients as almost cured, while four others remain unchanged.

Aristol was tried by three patients, partly internally, dissolved in ether, and partly externally, in the form of ointment ; the effect was the same as after the use of iodide of potassium, and it was stopped after three weeks' trial.

Naphthol and *Salol* were tried for a long time, but the effect was almost *nil.* Salol has also been used by Dr. Lütz in the Sandwich Islands, and by Surgeon Major Cook in Madras, but though some amelioration in the condition of the patients has been noted, no case has been cured.

Methylene Blue was given to one tuberous patient, both internally and hypodermically. The skin, especially the tubers, became deeply blue, but a microscopical examination showed the bacilli unaltered. The treatment was continued from May 20, 1891 till January 30, 1892. Some tubers diminished a little, but most of them became larger, so that the disease as a whole grew worse.

Nerve stretching was first tried by Dr. Gerald Bamfert, who stated that he had done the operation with success on an anæsthetic patient,

in whom both hands were atrophic and sensibility much diminished. The ulnar nerve was stretched and incised longitudinally. The sensibility in the right hand re-appeared immediately after the operation ; and after some days the muscular power was almost completely restored. In three anæsthetic patients in the Lungegaard's hospital the operation was performed ; the ulnar nerve was stretched and incised along a length of three to four inches. All went well, only the anæsthesia remained unchanged ; neither sensibility nor muscular power was restored. Dr. Beaven-Rake, who has done numerous nerve-stretchings in Trinidad, says, "on the whole the results of nerve-stretching for anæsthesia cannot be considered satisfactory."

Dr. Beaven-Rake has also done the operation for pains in the limbs, for which hypodermic injections of morphine have been successfully used in the Lungegaard's hospital.

Electricity, both faradic and galvanic, has been used for anæsthetic leprosy, and electric baths, but no good effect has been attained.

Surgical measures are often needed. Section of the cornea, as introduced by Dr. Boeckmann, in the case of tubers growing into it, has already been mentioned, as has the operation of tarsoraphia interna in ectropion of the lower eyelid. Iridectomy has often to be performed, when the

pupil has been obliterated by adhesions of the iris or by exudation.

Tracheotomy is necessary when the larynx is occluded by leprous growths or by cicatrices.

Necrotomies should always be performed when there is necrosis of the bones of the hands and feet. It is astonishing how well the wounds heal in the anæsthetic parts, and patients are spared from long-standing suppuration by the removal of the necrosed bones.

The best remedy for leprosy Dr. Danielssen found in his experience to be *Salicylate of soda.* If the patients were badly nourished, he first administered quinine, iron, cod-liver oil, and nutritious food, and when the patient's condition was satisfactory he gave 1·0 gramme salicylate of soda four times daily, and for six months or a year the dose was gradually increased. Its good effects were seen in both forms of the disease. In the maculo-anæsthetic form the patches and the less extensive anæsthesias slowly disappeared. In the tuberous form, when not of too long duration and severity, the rapidity of progress was diminished, and fresh eruptions were prevented. A complete cure has, however, not been attained, unless, at the same time, there have been applied regularly "cucurbita cruenta," steam baths, alternating with warm water and sea-water baths, exercise in the fresh air, good

hygienic surroundings, and good diet. From time to time irritants were applied, such as, carbolic and salicylic acids, in the form of fomentations and ointments. It is only in cases in the first six to twenty-four months that a favourable issue can be hoped for. The results of the treatment in the Lungegaard's hospital are nothing to boast of, but they show, according to Dr. Danielssen, that leprosy at its commencement can be cured. In our opinion this is true, but with the reservation that the cure is not due to the treatment, but is the natural development of the disease. We have seen cases of leprosy, in the country, both tuberous and maculo-anæsthetic, completely recover without any treatment whatever. So far as we know, in most of the patients discharged cured from the Lungegaard's hospital the anæsthesia has increased, which is in conformity with the general progress of the disease, the nerve fibres continuing to undergo atrophy from the pressure of the contracting inflammatory tissue in the nerve trunks, as described above.

Treatment ought theoretically to be directed to the destruction of the bacilli, and this is what Dr. Unna sought to attain by his reducing remedies, pyrogallic acid, chrysarobin, etc.; but while Dr. Unna and Dr. Deichmann succeeded in Hamburg, Dr. Danielssen had no success when

using the same remedies. Dr. Danielssen believed that the bacilli were destroyed by salicylate of soda ; but we fear that others will not succeed with this same remedy.

As we are then, in our opinion, unable to destroy the bacilli with remedies, either internal or external, it only remains to us to prevent infection, and that can only be attained by isolation of those affected. For this isolation no very costly measures are required. From what we saw in North America in 1888, all that is wanted is cleanliness, both personal, and in the household. But amongst the people where leprosy prevails, it is almost impossible to get sufficient cleanliness thoroughly enforced. We think, therefore, that the best measures are those which have been taken in Norway, where the lepers are isolated at their own request, and where the communities can get rid of the disease, if they will, since the sanitary authorities have the power to order the leper to live sufficiently isolated from his family, and, if he cannot or will not assent to this, can compel him to enter an asylum. At the same time, the doctrine of cleanliness and isolation and the necessity of their observance in order to prevent the spread of the disease, is constantly preached.

Since the state pays all the expenses of the lepers in the asylums, their families are generally

relieved by getting rid of the lepers, who are almost invariably bad workers and unable to earn their living.

These measures are quite adequate in a democratic country like Norway, where the communities have governed themselves since 1836, and the results are most satisfactory, seeing that we had in 1856, 2833 lepers, and at the end of 1890 only about 950, which number, when corrected, will probably amount to about 1100.

Whether the same measures would be adequate in other countries where leprosy prevails, we cannot of course say ; it must depend on the social condition of the community. But we are firmly convinced that isolation *must* be carried out in some appropriate fashion.

TABLES.

SHOWING THE FREQUENT COMPLICATION OF

No.	Duration of Disease in Years.	Lungs and Pleura.	Liver.
1	11	Normal.	Amyloid and leprous.
2	6	Left-sided tubercular pleurisy; in lower lobes, lobular pneumonia.	Leprous.
3	10	Hydro-thorax.	Amyloid and leprous.
4	5	Cavities in both apices; tubercular peri-bronchitis in the upper lobes.	Leprous.
5	12	Normal.	Amyloid.
6	8	Lobular pneumonia in the right lung.	Leprous.
7	13	Lungs œdematous.	Leprous.
8	7	In both lower lobes pneumonia, with commencing cavity formation.	Leprous.
9	5	In the left lung, cavities in the apex, and widespread lobular pneumonia. The same without cavity formation in the R.	Amyloid and leprous.
10	6	Œdema.	Leprous.
11	5	In upper lobes, cavities, and lobular pneumonia.	Amyloid and leprous.
12	11	Normal.	Leprous.
13	9	Cavities, tubercular peri-bronchitis, pleural tuberculosis.	Amyloid & leprous (?)
14	10	Normal.	Amyloid and leprous.
15	14	Tubercular peri-bronchitis and pleurisy.	Tubercular.
16	4	Tubercular peri-bronchitis and pleurisy.	Tubercular, amyloid, and leprous.

NODULAR LEPROSY WITH TUBERCULOSIS.

Spleen.	Kidneys.	Intestinal Canal.
Amyloid and leprous.	Fatty degeneration.	Amyloid.
Tubercular.	Fatty degeneration.	Normal.
Leprous.	?	Normal.
Amyloid.	Amyloid.	Amyloid and tubercular ulceration.
Amyloid.	Amyloid.	Normal.
Leprous.	Fatty degeneration.	Normal.
Leprous.	Fatty degeneration.	Normal.
Leprous.	Normal.	Normal.
Leprous.	Amyloid and fatty degeneration.	Amyloid.
Leprous.	Fatty degeneration.	Normal.
Amyloid and leprous.	Amyloid.	Amyloid.
Leprous.	Interstitial nephritis.	Normal.
Leprous (?).	Amyloid and tubercular.	Amyloid and tubercular, tubercular peritonitis.
Leprous.	Amyloid.	Amyloid ulceration in the ileum.
Tubercular.	Amyloid and tubercular.	Amyloid and tuberculosis of omentum and mesentery.
Tubercular and amyloid and leprous.	Tubercular and amyloid.	Amyloid, tubercular ulceration, mesenteric tuberculosis.

No.	Duration of Disease in Years.	Lungs and Pleura.	Liver.
17	7	Normal.	Leprous and amyloid.
18	10	Numerous cavities and gelatinous pneumonia.	Leprous and amyloid.
19	6	Numerous cavities and gelatinous pneumonia.	Leprous.
20	15	Normal.	Fatty.
21	2	Normal.	Leprous.
22	14	A small pneumonia in R.	Leprous.
23	7	Cavities, tubercular peri-bronchitis, and lobular pneumonia in left lung.	Leprous.
24	13	Bronchiectasis and lobular pneumonia.	Leprous.
25	8	Bronchiectasis and lobular pneumonia.	Leprous.
26	5	Normal.	Leprous.
27	?	Small cavities and lobular pneumonia.	Leprous and amyloid.
28	3	Small cavities and lobular pneumonia.	Leprous and tubercular.
29	1½	Tuberculosis of lungs and pleura.	Leprous and tubercular.
30	4	Caseous areas in both lungs.	Leprous.
31	6	Œdema, bronchitis.	Amyloid.
32	24	Lobular pneumonia.	Amyloid.
33	6	Cavities and lobular pneumonia.	Leprous and amyloid.
34	5	Normal.	Leprous.

Spleen.	Kidneys.	Intestinal Canal.
Leprous and amyloid.	Amyloid.	Amyloid.
Leprous and amyloid.	Fatty degeneration.	Peyer's patches and solitary glands tubercular with commencing ulceration.
Leprous.	Interstitial nephritis.	Ulcerating plaques and solitary glands.
Amyloid.	Amyloid.	Amyloid.
Leprous.	Normal.	Normal.
Leprous.	Amyloid and fatty degeneration.	Amyloid.
Leprous and amyloid.	Amyloid and fatty degeneration.	Tubercular ulceration.
Leprous.	Amyloid and fatty degeneration.	Normal.
Leprous.	Slight fatty degeneration.	Normal.
Leprous.	Slight fatty degeneration.	Normal.
Leprous and amyloid.	Amyloid.	Normal.
Leprous and tubercular.	Fatty degeneration and amyloid.	Amyloid ulcerated follicles and plaques.
Leprous and tubercular.	Acute nephritis, tuberculosis in R. kidney.	Normal.
Leprous.	R tubercular, L. hydronephrosis, tubercular cystitis.	Normal.
Amyloid.	Amyloid.	Amyloid.
Amyloid.	Amyloid and fatty degeneration.	Amyloid.
Leprous and amyloid.	Normal.	Amyloid.
Leprous and amyloid.	Amyloid and interstitial nephritis.	Amyloid.

No.	Duration of Disease in Years.	Lungs and Pleura.	Liver.
35	4	Pleuritic adhesions.	Leprous.
36	14	Œdema.	Amyloid.
37	4	L. Tubercular pleurisy; R. tubercular peri-bronchitis.	Amyloid.
38	6	Tubercular peri-bronchitis and lobular pneumonia; tubercular pleurisy in left lung.	Leprous.
39	6	Tubercular peri-bronchitis, lobular pneumonia and small cavities.	Leprous and amyloid.
40	7	Normal.	Leprous and amyloid.
41	8	Lobular pneumonia.	Leprous.
42	2	Tubercular.	Leprous and tubercular
43	12	Lobular pneumonia.	Leprous.
44	8	Lobular pneumonia, pleurisy.	Leprous and amyloid.
45	4?	Cavities and lobular caseous pneumonia.	Leprous and amyloid.
46	4	Tuberculosis, double pneumonia.	Leprous.
47	10	Œdema.	Amyloid.
48	4	Tuberculosis.	Tubercular and amyloid.
49	?	Normal.	Leprous and amyloid.
50	4	Tuberculosis, numerous large cavities, tubercular pleurisy.	Leprous.
51	7	Bronchiectasis, lobular pneumonia.	Leprous.
52	?	R. lobular pneumonia.	Leprous.
53	?	Pleuritic adhesions, lungs normal.	Amyloid.
54	5	Tuberculosis of lungs and pleura.	Leprous, tubercular, and amyloid.

Spleen.	Kidneys.	Intestinal Canal.
Leprous.	Normal.	Peritonitis, ulceration of the vermiform process.
Normal.	Amyloid and fatty degeneration.	Amyloid.
Amyloid and tubercular.	Tubercular.	Amyloid, tubercular peritonitis.
Leprous.	Normal.	Amyloid, localised tubercular peritonitis around the spleen.
Leprous and amyloid.	Tubercular and amyloid.	Amyloid.
Leprous and amyloid.	Amyloid.	Normal.
Leprous and amyloid.	Amyloid.	Normal.
Leprous and tubercular.	Normal.	Tubercular ulceration.
Leprous.	Amyloid and fatty degeneration.	Normal.
Leprous and amyloid.	Acute nephritis.	Normal.
Leprous and amyloid.	Normal.	Amyloid ulcerations.
Leprous.	Normal.	Normal.
Amyloid.	Amyloid.	Amyloid.
Amyloid.	Tubercular and amyloid.	Amyloid, tubercular ulcerations.
Leprous and amyloid.	Amyloid.	Amyloid.
Leprous.	Normal.	Tubercular ulceration.
Leprous.	Normal.	Normal.
Leprous.	Normal.	Normal.
Amyloid.	Amyloid.	Amyloid.
Leprous and tubercular.	Amyloid.	Amyloid, tubercular ulceration.

No.	Duration of Disease in Years.	Lungs and Pleura.	Liver.
55	12	Pleuro-pneumonia on right side, hydro-thorax sinistra, hydro-pericardium, ascites.	Leprous. (?)
56	3	Tuberculosis.	Cirrhosis.
57	13	Normal.	Normal.
58	7	Apical tuberculosis.	Leprous.
59	21	Œdema.	Leprous (?).
60	2	Tuberculosis, cavities.	Amyloid.
61	10	Normal.	Fatty.
62	9	Croupous pneumonia.	Amyloid.
63	7	Œdema.	Leprous.
64	7	Lobular pneumonia.	Normal.
65	9	Normal.	Leprous.
66	3	Tuberculosis.	Leprous.
67	?	Double pleurisy, caseous node of the size of a walnut in the left lung.	Fatty.
68	?	Marked stenosis of larynx. Both apices infiltrated.	Leprous.
69	?	Tuberculosis.	Normal.
70	?	Normal.	Leprous and amyloid.
71	?	Normal.	Leprous.
72	17	Normal.	Cancerous.
73	7	Tuberculosis.	Leprous and amyloid.
74	?	Tuberculosis of lungs and pleura.	Tubercular.
75	?	Œdema.	Amyloid.

Spleen.	Kidneys.	Intestinal Canal.
Leprous (?) commencing amyloid degeneration.	Nephritis.	Amyloid.
Leprous (?)	Normal.	Normal.
Normal.	Amyloid.	Normal.
Leprous.	Interstitial nephritis.	Normal.
Leprous (?).	Parenchymatous nephritis.	Normal.
Amyloid.	Amyloid and tuberculosis.	Tubercular.
Normal.	Parenchymatous nephritis.	Tubercular (?)
Amyloid.	Amyloid.	Normal.
Leprous.	Normal.	Hyperæmia.
Leprous.	Normal.	Normal.
Leprous.	Parenchymatous nephritis.	Normal.
Leprous.	Congested, otherwise normal.	Normal.
Tubercular.	?	Normal.
Leprous.	Normal.	Normal.
Normal.	Interstitial nephritis.	Normal.
Leprous and amyloid.	Parenchymatous nephritis.	Normal.
Leprous.	Interstitial nephritis.	Normal.
Leprous.	Normal.	Normal.
Leprous and amyloid.	Amyloid.	Normal.
Tubercular.	Tubercular.	Tubercular.
Amyloid.	Amyloid.	Amyloid.

No.	Duration of Disease in Years.	Lungs and Pleura.	Liver.
76	2-3	Tuberculosis.	Tubercular & amyloid.
77	?	Tuberculosis.	Leprous.
78	10	Tuberculosis.	Leprous and amyloid.
79	7	Cavities.	Leprous and amyloid.
80	?	Cavities.	Leprous & tubercular.
81	7	Normal.	Leprous and amyloid.
82	?	Double pneumonia.	Amyloid.
83	?	Normal.	Leprous.
84	?	Œdema.	Leprous and cancerous.
85	?	Œdema.	Leprous and amyloid.
86	?	Tuberculosis.	Leprous.
87	$1\frac{1}{2}$	Tuberculosis.	Leprous and tubercular
88	?	Normal.	Leprous and amyloid.
89	?	Tuberculosis.	Leprous and amyloid.

Spleen.	Kidneys.	Intestinal Canal.
Leprous and amyloid.	Amyloid.	Tubercular, tubercular peritonitis.
Leprous and tubercular.	Normal.	Tubercular.
Leprous.	Amyloid.	Amyloid.
Amyloid.	Parenchymatous nephritis.	Normal.
Leprous and tubercular.	Normal.	Tubercular.
Leprous and amyloid.	Amyloid.	Amyloid.
Amyloid.	Parenchymatous nephritis and amyloid.	Amyloid.
Leprous.	Normal.	Amyloid.
Leprous.	Interstitial nephritis.	Normal.
Leprous and amyloid.	Interstitial nephritis and amyloid.	Normal.
Leprous and tubercular.	Normal.	Tubercular.
Leprous and tubercular.	Normal.	Tubercular.
Leprous.	Parenchymatous nephritis.	?
Leprous.	Interstitial nephritis and amyloid.	Normal.

THE PROPORTION OF TUBERCULOSIS

No.	Brain.	Spinal Cord.	Lungs.
1	Nothing.	Nothing.	Tubercular.
2	Nothing.	Nothing.	Tubercular.
3	Hydroceph. internus. Thickening of the pia mater. Gelatinous exudation between pia and arachnoid.	Nothing.	Tubercular.
4	Nothing.	Not examined.	Tubercular.
5	Nothing.	Not examined.	Normal.
6	Nothing.	Not examined.	Normal.
7	Solitary tubercle in the cerebellum. Hydroceph. internus.	——	——
8	——	Not examined.	Normal.
9	——	Not examined.	Tubercular.
10	Hydroceph. internus.	Not examined.	Tubercular.
11	Normal.	Not examined.	——
12	Normal.	Not examined.	Tubercular.
13	Tubercular meningitis.	Not examined.	Miliary tuberculosis.

N MACULO-ANÆSTHETIC LEPROSY.

Liver.	Spleen.	Kidneys.	Nerves.
nlargement and hyperæmia.	Nothing.	Hyperæmia.	Ulnar nerve thickened in the under third of the upper arm.
othing.	Nothing.	Enlargement and fatty degeneration.	——
tty.	Nothing.	Nothing.	Ulnar nerve thickened throughout a length of about 10-15 c.m. about the elbows. Median nerve thickened at the wrist.
tty.	Normal.	Fatty degeneration.	——
tty.	Normal.	Fatty degeneration.	——
ormal.	Normal.	Granular, atrophic. Fatty degeneration.	——
——	——	Tuberculosis of the left kidney.	——
tty.	——	Fatty degeneration.	Ulnar nerve as thick as a little finger.
iberculosis of peritoneum. Liver amyloid.	Amyloid.	Hyperæmia. Fatty degeneration.	Ulnar nerve contracted.
ibercular.	Normal.	Normal.	——
nyloid.	Amyloid.	Amyloid.	——
ypertrophic.	Abscess.	Abscess.	——
iliary tuberculosis.	Miliary tuberculosis.	——	——

No.	Brain.	Spinal Cord.	Lungs.
14	——	Degeneration of the posterior columns.	——
15	——	——	——
16	Hydroceph. internus.	Normal.	Normal.
17	Normal.	Lumbar cord thickened, the membranes thickened and hyperæmic.	Normal.
18	Normal.	Thin, atrophic (?)	Normal.
19	——	——	——
20	——	——	——
21	——	——	——
22	——	——	Tubercular.
23	Normal.	Normal.	——
24	Normal.	Normal.	Double pleurisy.
25	Sero-purulent meningitis.	Normal.	——
26	Normal.	Normal.	——
27	Normal.	Normal.	——
28	——	——	Tubercular.
29	Normal.	Normal.	——

Liver.	Spleen.	Kidneys.	Nerves.
ty and amy-oid.	Amyloid.	Fatty degeneration and amyloid.	Ulnar nerve sclerotic.
ty and amy-oid.	Amyloid.	Fatty degeneration and amyloid.	Ulnar nerve sclerotic.
pertrophy (?)	——	——	——
rmal.	Normal.	Normal.	——
ge.	Normal.	Normal.	Axillary plexus atrophic. Ulnar and radial nerves thickened.
yloid. Intestine also amyloid.	Amyloid.	Interstitial nephritis.	——
——	Amyloid.	Amyloid.	——
——	——	Interstitial nephritis.	Ulnar nerve sclerosed.
yloid.	——	——	——
——	——	——	——
——	——	——	——
ty degeneration.	——	——	——
——	——	——	——
——	——	——	——
ty degeneration.	Tubercular.	——	——
testine also	tubercular.)		
yloid.	Amyloid.	Fatty degeneration.	——

No.	Brain.	Spinal Cord.	Lungs.
30	Normal.	Normal.	——
31	——	——	Tubercular.
32	——	——	Tubercular.
33	——	——	——
34	——	——	Croupous pneumonia.
35	——	——	Tubercular.
36	——	Degeneration of the posterior columns. Atrophy of the posterior roots. Sclerosis of the spinal ganglia.	——

Liver.	Spleen.	Kidneys.	Nerves.
Amyloid.	Amyloid.	Amyloid.	Ulnar nerve contracted.
Normal. (Intestine also	Normal. tubercular.)	——	——
Amyloid.	Amyloid.	Nephritis parenchymatous.	——
Fatty. (Intestine also	Normal. tubercular.)	Tuberculosis of the left kidney.	——
——	——	Cirrhotic kidney.	——
Tuberculous.	Tuberculous.	Fatty degeneration. Amyloid.	——
——	——	——	——

TABLE III.—THE PROPORTIONS OF THE TWO FORMS OF LEPROSY.

	Of every Hundred Lepers from 1856 to 1890 there belonged to the Nodular Form:			Maculo-anæsthetic Form:		
	Altogether.	Males.	Females.	Altogether.	Males.	Females.
In the Eastern part of Norway -	47·7	26·6	21·1	52·3	27·5	24·8
Littoral Districts.						
Lister and Mandal - -	58·8	41·2	17·6	41·1	29·4	11·7
Stavanger - - - -	60·6	34·7	25·9	39·3	21·0	18·3
Söndre Bergenhus - -	68·0	34·2	33·8	31·9	15·3	16·6
Nordre Bergenhus - -	66·8	34·9	31·9	33·0	17·2	15·8
Romsdal - - - -	73·3	44·4	28·9	27·2	15·8	11·4
Söndre Trondhjem - -	74·3	48·5	25·8	25·7	16·4	9·3
Nordre Trondhjem - -	70·6	46·8	23·8	29·5	17·4	12·1
Nordland - - - -	71·5	44·1	27·4	28·5	17·1	11·4
Tromsö - - - -	79·1	52·9	26·2	20·9	13·1	7·8
Finmarken - - - -	82·5	65·0	17·5	17·5	12·5	5·0
Sogn - - - - - - -	56·6	31·8	24·8	43·4	23·0	20·4
Söndfjord - - - - -	72·6	37·4	35·2	27·4	14·3	13·1
Nordfjord - - - - -	68·5	33·9	34·6	31·3	16·9	14·4

THE RESULTS OF ISOLATION IN NORWAY.

Year.	Total at commencement of Year.	New Cases.	Result.			Number at end of Year.		Total at end of Year.
			Died.	Cured.	Emigrated.	At Home.	In Asylums	
1856	—	238	?	?	?	2598	235	2833
1857	2833	242	293	3	15	2339	427	2766
1858	2766	210	224	3	3	2294	475	2769
1859	2769	239	213	8	7	2267	523	2790
1860	2790	219	251	1	6	2218	539	2757
1861	2757	219	239	6	14	2028	711	2739
1862	2739	211	215	5	11	2009	698	2707
1863	2707	196	192	5	4	1947	749	2696
1864	2696	201	202	—	8	1914	781	2695
1865	2695	201	205	5	8	1910	772	2682
1866	5682	203	214	3	10	1879	795	2674
1867	2674	200	191	8	4	1876	787	2663
1868	2663	206	210	6	7	1865	788	2653
1869	2653	183	199	10	13	1820	787	2607
1870	2607	187	203	4	13	1762	764	2526
1871	2526	170	238	2	16	1681	747	2428
1872	2428	131	205	5	10	1627	708	2335
1873	2335	129	177	9	17	1592	672	2264
1874	2264	137	183	6	9	1566	643	2209
1875	2209	134	203	5	14	1499	623	2122
1876	2122	115	187	3	6	1440	613	2053
1877	2053	110	163	3	7	1372	629	2001
1878	2001	105	149	10	8	1341	618	1959
1879	1959	88	162	5	10	1277	602	1879
1880	1879	72	150	7	7	1178	617	1795
1881	1795	60	164	5	8	1092	608	1692
1882	1692	66	137	11	7	1061	553	1614
1883	1614	87	127	9	5	1022	535	1557
1884	1557	55	140	10	2	944	519	1463
1885	1463	71	146	9	12	855	522	1377
1886	1377	48	135	16	9	748	522	1270
1887	1270	47	111	2	3	704	514	1218
1888	1218	27	99	8	1	631	524	1156
1889	1156	27	86	9	12	551	530	1081
1890	1081	10	122	6	2	447	507	954

PLATE VI.

PLATE VI.

Fig. 1.—Two cells from a fresh nodule in 1 per cent. osmic acid (Gundlach, No. viii).

Fig. 2.—Part of a section of a cutaneous leproma. Round cells with clear stellate cells between them (Hartnack, No. ix).

Fig. 3.—From a corneal leproma. Round cells with corneal corpuscles between them (Hartnack, No. ix).

Fig. 4.—From the border of a corneal leproma. Capillary surrounded by round cells. Müller's Fluid (Hartnack, No. ix).

Fig. 5.—From the inside of a corneal leproma. A capillary surrounded by round cells in among globi and corneal corpuscles unchanged or filled with brown granules. Müller's Fluid (Hartnack, No. ix).

Fig. 6.—The brushed-out net-work of a cutaneous leproma (Hartnack, No. ix).

Fig. 7.—From a corneal leproma. Capillary surrounded by round cells free from bacilli, and outside these, cells filled with bacilli. Seibert homogen. immersion $\frac{1}{18}$.

Fig. 8.—Cells from a cutaneous leproma. Eosin, Bismarck brown, and Gentian-violet. Hardening in Fleming's Solution. Seibert homogen. immersion $\frac{1}{18}$.

Fig 1

Fig 2

Fig 3

Fig 4

Fig 5

Fig 7

Fig 8

PLATE VII.

PLATE VII.

Fig. 1.—Cells and globi from cutaneous lepromata. Müller's Fluid (Hartnack, No. ix).

Fig. 2.—Globi from a leprous spleen.

Fig. 3.—Two globi from the retina.

Fig 1

Fig 2

a b c

d e f

g h k

Fig 3

x

x'

PLATE VIII.

PLATE VIII.

Fig. 1.—Corneal corpuscles filled with brown granules (Hartnack, No. ix).

Fig. 2.—From a leproma of the iris. Round cells with stellate cells (Hartnack, No. ix).

Fig. 3.—Corneal space with round cells near the corneal corpuscles (Hartnack, No. ix).

Fig. 4.—Cells with two nuclei full of bacilli from a cutaneous leproma. Seibert homog. immersion $\frac{1}{16}$.

Fig. 5.—Two cells with bacilli from a leprous spleen. Fuchsin, methyl-blue. Seibert homog. immersion $\frac{1}{16}$.

Fig. 6.—From a leprous liver. White blood corpuscles with bacilli in a capillary. Seibert homog. immersion $\frac{1}{16}$.

Fig 1.

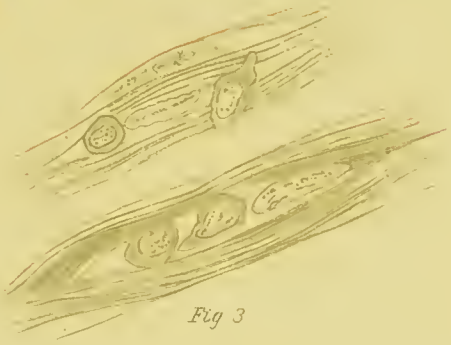


Fig 3

Fig 2

Fig 4

Fig. 5.

Fig 6

PLATE IX.

PLATE IX.

Fig. 1.—From a leprous liver. Bacilli in an endothelial cell of a capillary. Seibert homog. immersion $\frac{1}{16}$.

Fig. 2.—Piece of a very leprous liver. Capsule below, cut surface above.

Fig. 3.—Cut surface of a very leprous spleen.

Figs. 4 and 5 and *Plate X*, *Fig.* 1.—Cross section of the seminal canals with bacilli around the nuclei of the walls and in the epithelium; in *Plate X*, *Fig.* 1, is shown an epithelial cell filled with bacilli.

Fig 1.

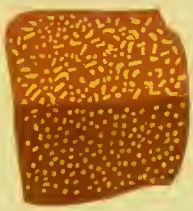
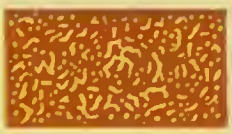
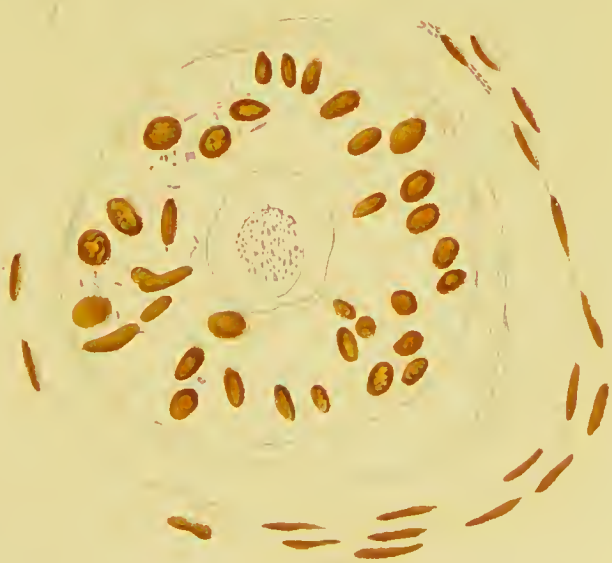


Fig 2

Fig 4



Fig



Fig

PLATE X.

PLATE X.

Fig. 1.—Epithelial cell from a seminal canal, filled with bacilli.

Fig. 2.—A globus with a vacuole in which are fragments stained with Bismarck brown, probably the remains of nuclei.

Fig. 3.—A globus lying in a cell; the nucleus and a part of the cell-protoplasm preserved.

Fig. 4.—An epithelial cell from a seminal canal, filled with bacilli broken down into granules.

Fig. 5.—Cross section of a blood-vessel with bacilli in the endothelium and a white blood corpuscle filled with bacilli.

Fig. 6.—Longitudinal section of a blood-vessel showing bacilli in the endothelium, and a fibrinous coagulum enclosing two white blood corpuscles, one of them filled with bacilli.

Fig. 7.—Bacilli free between the red blood corpuscles.

Fig. 8.—A connective tissue space from the tunica albuginea filled with bacilli.

Fig. 9.—Cross section of a blood-vessel with bacilli around the nuclei of the surrounding connective tissue.

All the preparations from the testicle were hardened in Fleming's or Müller's solutions, and the drawings made with a Seibert homog. immersion lens $\frac{1}{16}$. *Plate IX*, *Fig.* 5 with Seibert $\frac{1}{8}$.

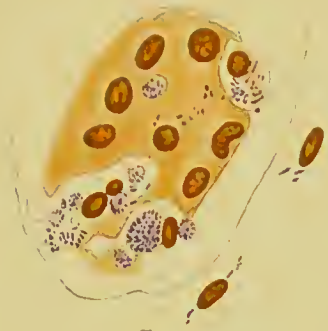


Fig 1

Fig 2

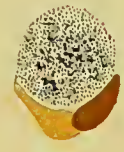


Fig. 3.

Fig 4

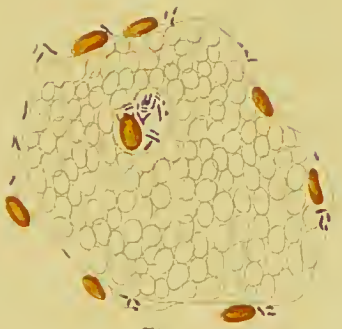


Fig 5.

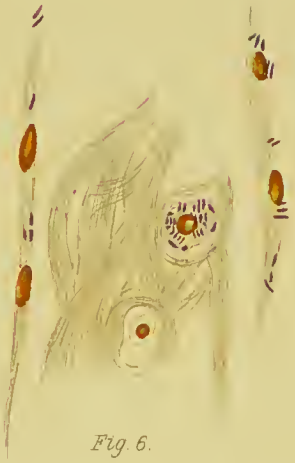


Fig. 6.

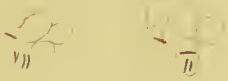


Fig 7

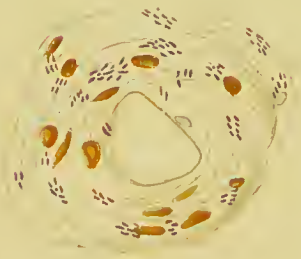


Fig. 9.

Fig 8

SCOTT & FERGUSON, EDINR.

PLATE XI.

PLATE XI.

Fig. 1.—Bundle of nerve fibres from a ciliary nerve, the cells of Schwann's sheath filled with brown granules.

Fig. 2.—The myelin sheath pressed in by a cell filled with granules.

Fig. 3.—Section from an old leprous macule.

Fig. 4.—Section from a recent leprous macule.

Both sections stained with Fuchsin and Methyl-green. Seibert homogen. immersion $\frac{1}{18}$.

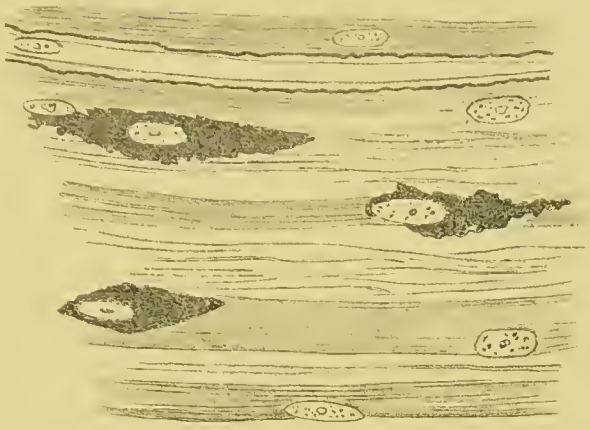


Fig. 1.

Fig. 2.

Fig 3

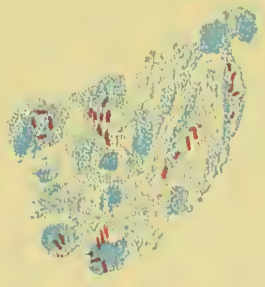


Fig 4

PLATE XII.

PLATE XII.

Fig. 1.—Cross section of a leprous ulnar nerve. The darkly hatched cells represent those filled with brown granules. It will be noted that the axial cylinder is wanting in many of the nerve fibres (Hartnack, No. ix).

Fig. 2.—A piece of neurilemma with flat connective tissue cells lying on it, containing brown granules darkened by osmic acid (Gundlach, No. viii).

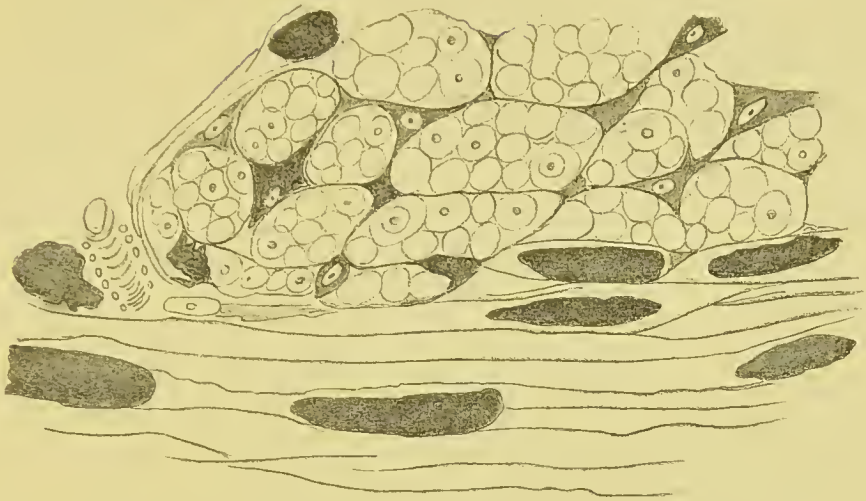


Fig 1

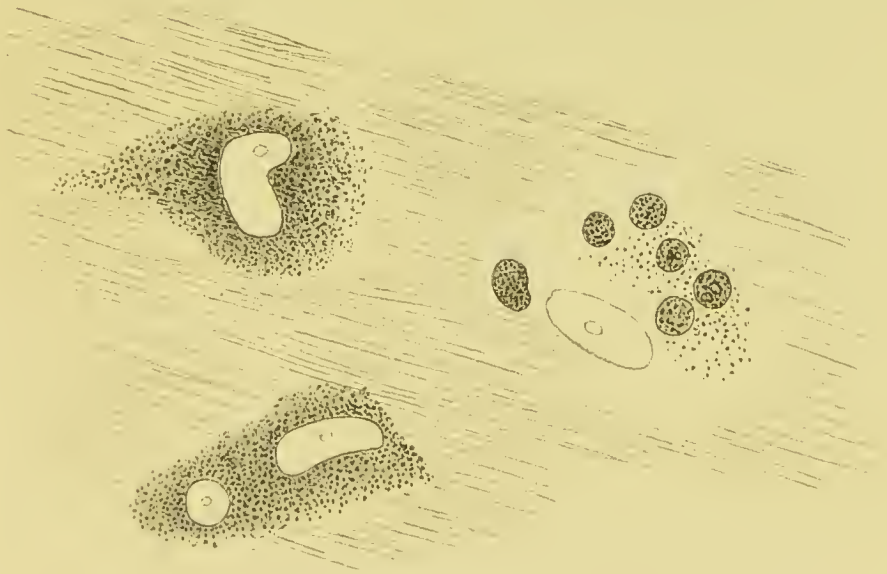


Fig 2

SCOTT & FERGUSON, EDIN.

PLATE XIII.

PLATE XIII.

Fig. 1.—Cross section of an atrophic muscle, growth of nuclei in the perimysium. Low power.

Fig. 2.—Cross section of an atrophic muscle with great development of connective tissue. Low power.

Fig. 3.—Proliferation of the nuclei of the perimysium. High power.

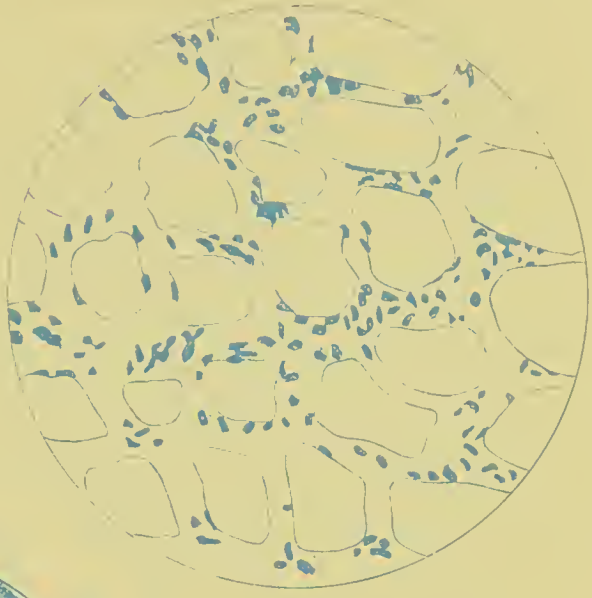


Fig 1

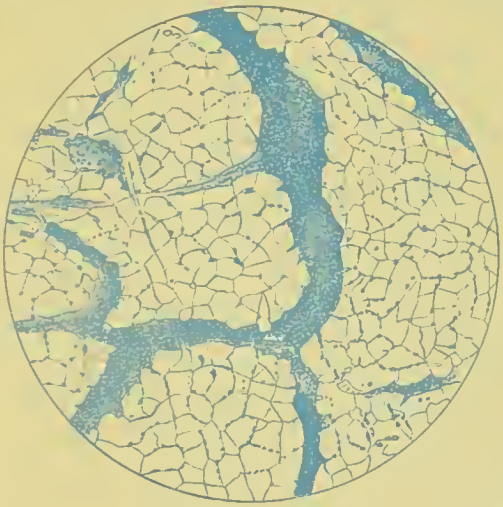


Fig 2.

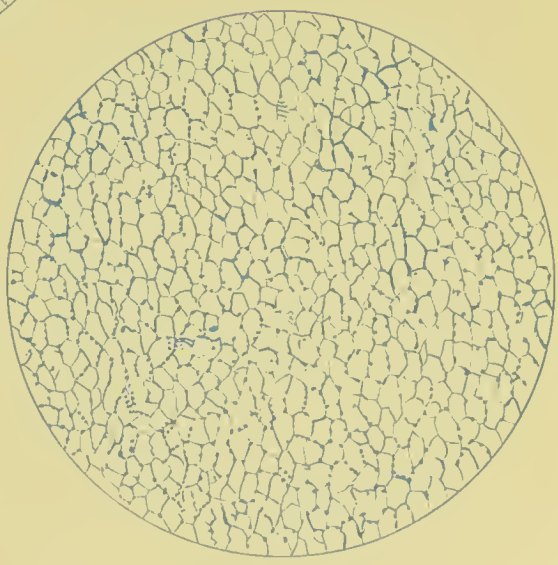


Fig .

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